

THE PRACTITIONER

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EDITORIAL

The year 1948 will be a momentous one in the life of *The Practitioner* and in the lives of many of its readers. It finds a world still suffering from the effects of the recent conflict, from the disruption of communications, the dislocation of industry, and the weariness which that conflict brought in its train; yet it finds in every country men of good will who seek peace upon earth. It sees the discovery of new means of destruction, while at the same time inventions meant to destroy, such as the nitrogen mustards, are being turned to the fight against disease. In this year *The Practitioner* celebrates its eightieth birthday, and never in those eighty years has the journal shown more manifestly those attributes of youth—health, growth, and an ability to face the future with hopeful optimism.

Two new features mark the entry of *The Practitioner* upon its eightieth year. One is the step that is being taken to assist in the maintenance of the link which developed between British and American medicine during the 1939-45 war. The war saw the happy collaboration of the Armed Forces and industrial organizations of the great English speaking nations in final victory, and the equally important collaboration of the Medical Services and Research Departments of the same countries towards the victory over disease and suffering. British, American, Canadian, Australian, New Zealand, South African and Indian doctors got to know each other; they learned that each had something to give the other, that American drive and British caution are not incompatible schools of thought, but complementary qualities that can be fruitfully combined to the solution of common problems. The war over, they are loth to slip back into continental isolation.

Arrangements have been made whereby the well-known firm of Charles C Thomas of Springfield, Illinois, will undertake the distribution of *The Practitioner* in the American Continents. In order to keep the editorial board in touch with developments in America, Dr. Robert M. Stecher of Western Reserve University Medical School, Cleveland, has been appointed Associate Editor in America. Dr. Stecher, a man well known for his literary interests and his wide circle of friends in every branch of practice, will also arrange for the publication in *The Practitioner* of articles by leading members

of the profession in America. In addition to American contributions to the symposia which have for so long been a valued feature of the journal, it is proposed to publish a series of articles dealing with current medical practice in America. The first of these, by Colonel Hargreaves on "Trends in American Medicine", appears in this issue, and it is to be followed by one on "Present-day Surgical Practice in the United States", by Dr. Alton Ochsner, Professor of Surgery in Tulane University, New Orleans.

The second new feature is the series on "Current Therapeutics" which begins in this issue with an article on "Folic Acid" by Professor L. J. Davis. For the general practitioner, and even for the consultant, it is proving increasingly difficult to keep pace with the rapidly changing face of medicine, particularly in the field of treatment. Therapeutics has always been the sphere upon which *The Practitioner* has laid special emphasis, and it is the aim of the editors in this coming year to ensure that through its pages practitioners shall obtain an authoritative interpretation of the significance and practical implications of current advances in medicine and surgery in all branches.

To mark the coming into force of the new Health Act, one of the most momentous events in the history of British medicine, it is proposed to publish later in the year a symposium on "Social Medicine". This will include articles dealing with the implications of the new Act as well as a series outlining the organization of medical practice in other lands. Whatever may be the merits or demerits of the new regime under which we in Great Britain have to practise the art of medicine, it is clearly essential, in order to maintain a sense of proportion, that we should be able to correlate this with the experiences of our colleagues in the Dominions, in America and on the continent of Europe.

In common with every other journal we are suffering from the paper shortage. In order to meet as many as possible of the requests from new subscribers, only one Special Number will be published this year. This decision has been taken with considerable reluctance, but in the circumstances it is the solution which will allow the best use to be made of our restricted supplies.

In spite of all the difficulties which we have had to contend with during 1947, and which clearly await us during 1948, we face the new year with confidence and enthusiasm. Our aim will be to maintain, to the best of our ability, those high standards of service which have been handed down to us by our predecessors in the editorial chair during the last eighty years. We trust that we shall continue to receive the cooperation of readers who by their suggestions and criticisms, both constructive and destructive, play such an important part in the development of the journal.

H. O.
W. T.

THE ENGLISHMAN'S FOOD TO-DAY

By SIR JACK DRUMMOND, D.Sc., F.R.I.C., F.R.S.

Formerly Scientific Adviser to the Ministry of Food.

HUNGER was not unknown in this country ten or fifteen years ago, when the effects of the depression of the thirties were apparent everywhere, but with the reassuring experience of the war years behind us it is shocking to realize that we are again facing the probability that many may not be able to fill their bellies this winter and the coming spring. Before examining how this deplorable situation has arisen and predicting what are likely to be its consequences it is necessary to present a background to the picture as a whole.

THE SUPREME IMPORTANCE OF CALORIES

One fact must be constantly borne in mind in looking at our food situation to-day, or indeed that of the world as a whole. The dominating consideration concerns the problem of providing the energy needs of the population. All other nutritional problems are relatively unimportant. Bayliss's famous aphorism, "Look after the calories and the proteins will look after themselves", was never more appropriate to the situation. It is therefore important that in responsible circles there should be proper appreciation of the significance of calorie estimates and calorie requirements. That this is often not the case is indicated by the many statements by politicians and in letters to the press that reveal an ignorance that would bring disgrace on a second year medical student. That, at least, is the most charitable view to take of them. For example, to draw conclusions from a comparison of the current "all-over" food supply calorie equivalence of 2,700 per head per day, with the estimated intake of 2,900 calories by an unemployed man before the war is completely misleading. Such comparisons are, in fact, meaningless, as will appear from what follows.

What are the facts? The energy needs of an individual are determined in the first place by age, sex, weight and constitution. These determine the basic needs. In addition, there is the energy required to enable the physical work of the day to be carried out. The total expenditure, and therefore the requirement, can be determined with great precision.

For groups of comparable individuals an average figure can be derived. Obviously, it will be less accurate an assessment than that for the individual, but the larger the group the more likely it is that the carefully selected estimate will approximate to the peak of the distribution curve representing the range, and it is a wide range, of calorie needs of all those comprising the group. Having divided the population into suitable groups, as shown in table 1, it is a simple matter to derive a weighted calorie figure representing the *per capita* need of the population as a whole.

TABLE I

							Calories per day
<i>Child</i>	under 1 year	800
	1- 3 years	1200
	4- 6 years	1600
	7- 9 years	2000
	10-12 years	2500
<i>Girl</i>	13-15 years	2600
	16-20 years	2400
<i>Boy</i>	13-15 years	3200
	16-20 years	3800
<i>Woman</i>	Moderately active	2500
	Hard work	3000
	Pregnant, nursing	2500-3000
<i>Man</i>	Moderately active	3000
	Hard work	4500

It is important to understand that this *per capita* figure is an estimate of the *need* of the body for energy; in other words, food that will provide the body with that energy must actually be eaten.

For the United Kingdom the figure derived by this calculation is 2,550 calories per-head per day; much the same figure is derived from examination of the corresponding data for the U.S.A. and for Canada. Fully covered by this comprehensive figure is the whole wide range from the 800 calories a day needed by infants to the 5000 calories expended by a woodman felling timber in a hard winter. To provide this energy expenditure more than the bare calorie equivalence in food is needed because allowance must be made for wastage in market, shop and home. Before the war this represented over 15 per cent. of the total food supply. During the war this loss was reduced to less than 10 per cent.; a commendably low proportion and one that could not easily be brought still lower. Wastage remains at about the same level to-day: one notes in contrast, that more than 20 per cent. of the food of the United States is wasted.

During the course of the war years the food supply available to the civilian population of the U.K. represented between 2,800-2,900 calories per head per day. There is clear evidence from records of body weight, from domestic food surveys and from industrial production levels that the calculated requirements of 2,550 calories were fully met.

BREAD AND POTATOES

From the standpoint of energy provision it is true to say that the salvation of the country during those war years was the unrestricted supply of bread and potatoes. It is a cardinal feature of an "efficient" rationing system that there shall be available a "reservoir" of energy to which all can turn to make

up their balance of calories. For obvious reasons this "reservoir" should consist of cheap and generally popular foods. We were therefore fortunate that for the entire period of the war it was possible to keep bread and potatoes outside the rationing system. In making dietary surveys during the war years it was common to find that adolescents and heavy manual workers ate as much as $1\frac{1}{4}$ lb. of bread and 1 lb. of potatoes a day. That was how they made up their total calorie intake to the requisite 3,500-4,500. There was no alternative. Of course, it meant eating bulky and unattractive meals, but at least there was no hunger.

There is another point that should be made before passing from this discussion of *per capita* calorie figures representing large groups or entire populations. They are significant in viewing the nutritional picture only if distribution of the staple foods is equitable. When there is not an effective rationing system, or when a flourishing black market diverts a great deal of food from control, inequalities of consumption will arise that may cause the poor to go hungry. Examples of these conditions are provided by Eire and by France, respectively.

There was a small margin of safety when a total food supply equivalent to about 2,850 calories per head per day was available to provide the working requirement of 2,550 calories. The unpleasant necessity of enforcing rationing of bread in the summer of 1946 seriously undermined the position that had been maintained with a narrow margin of security throughout the war. This restriction threw the whole responsibility for providing a "pool" of energy upon potatoes, a notoriously unreliable commodity. It was predictable that potatoes would be unlikely fully to meet the case and that, in consequence, many with high energy requirements, such as adolescents and heavy manual workers, would feel the pinch. There is evidence drawn from the experience of the past twelve months that this has occurred. The body weight records of adolescents are rather disturbing. Failure to gain weight and actual loss of weight are not uncommon among these boys and girls to-day.

But bad as bread rationing was, there was worse to come. I am reminded of a remark made to me during the darkest days of the war by an American friend: "You know, there are times when everything goes wrong; when things seem to go steadily from bad to worse. Then, suddenly, for no apparent reason, everything takes a turn for the worse". The deteriorating food situation has recently necessitated the rationing of potatoes. This is a most serious matter. There is no longer available a "pool" of energy in the form of a cheap, unrestricted supply of a popular food. It is no exaggeration to say that from the nutritional aspect the food situation has become precarious. An immediate effect of the latest restrictions has been to reduce the calorie equivalence of the total food supply to about 2,700 per head per day. Even with perfect distribution it is doubtful whether that would provide the 2,550 required to keep the nation working as it has been working.

If one also takes into account the probability that the severe food restrictions now operating will cause the black market to expand and flourish to a really formidable extent, there is cause for grave anxiety.

Experience in Europe during the past five years has demonstrated how soon an extensive black market trade in potatoes is established when bread is also restricted in supply. The people of Paris, Brussels and the other large towns of France and Belgium, survived the occupation, little the worse for the unpleasant experience, because they hoodwinked the Germans over potatoes, and understandably the Germans are deceiving us in precisely the same manner to-day. The fact that the nutritional status of the townsfolk of the Western Zone of Germany is steadily improving to-day is a tribute to the skill and cunning by which they are able to add 500-1000 calories daily, mainly in the form of potatoes, to the 1,500 or so provided by their bare rations.

What will be the consequences if we are unable to obtain sufficiently large supplies of wheat from the Soviet Union or elsewhere to enable the Government to abolish bread rationing? There is no doubt whatever that, as matters now stand, many will be unable to satisfy their demand for energy with the current rations. In particular, those with the higher levels of energy requirement will not be able to appease hunger.

It is all too easy to predict what will happen. Those who saw Western Europe as it was liberated have the picture clearly in perspective. There, too, it was primarily a picture of simple calorie deficiency. Complications due to lack of protein and specific vitamin deficiencies were seen only when the basic calorie intake was reduced to about 1,700 or less. Less serious calorie shortage, say within the range of 2000-2,200, affected growing boys and girls, particularly the older ones, and adolescents, by retarding their growth and reducing their power of concentration while at work. Adults tended to lose weight gradually and their physical output fell. Grumbling and irritability became much more pronounced, but the extraordinary listlessness and apathy of the calorie-starved individual was not seen until the intake fell below 1,500. Delayed or suppressed menstruation was a common sign among girls and young women in Western Europe during the occupation, but from evidence collected there it seems unlikely that this disorder will become common unless the all-over calorie level falls a good deal below 2,500.

Pregnant and nursing women form another vulnerable group. They should not suffer from the effects of the current food cuts unless they fail to take full advantage of their priority allowances, or sacrifice, as they so often do, part of their own food to help other members of the family. But it would be well to be on the watch for a retrogression in respect of the incidence of anæmia among adolescent girls and the younger women. This condition, in a mild form, was very common in the large towns of Western Europe in 1944-45. It was clearly not primarily due to iron deficiency be-

cause there was plenty of iron provided by the bread and vegetables of what was predominantly a vegetarian diet. It seemed much more likely that it was a sign of protein deficiency. It disappeared rapidly when there was more to eat. Apart from this possibility it is unlikely that the restricted diet on which we are obliged to subsist to-day will lead to the appearance of marked signs of deficiency disorders attributable to lack of vitamins or mineral elements.

Perhaps a reservation should be made in regard to ascorbic acid. During the war, both for us and for the inhabitants of Western Europe, *potatoes were vitamin C*. Few other vegetables came into the picture, which was entirely dominated by the potato supply. The current ration of potatoes, supplemented by other vegetables and by larger quantities of fruit than we had in the war years, may just see us through a critical late winter and spring, but it may be touch and go. If, on the other hand, the distribution of our inadequate potato supplies breaks down for any reason, and it is quite on the cards that it will fail in the early months of this year, the supply of vitamin C may reach danger levels, particularly in areas where the consumption of other sources of the vitamin is relatively small, as is the case in many Scottish industrial areas.

One of the most impressive lessons learned from war-time experience was the clear demonstration of the protective value of a diet comprising considerable proportions of bread made from a large part of the grain, and vegetables, including potatoes. War economy usually enforces consumption of long-extraction flour. Hungry people do all they can to supplement meagre rations with all the vegetables they can acquire by hook or by crook. The tendency is for vitamin intakes to be greater, not less, than in ordinary times. It must also be borne in mind that the need of the body for at least one, and possibly two more of the B vitamins, is reduced as the calorie intake falls. That is why vitamin deficiency conditions were so rarely encountered in Western Europe when relief came. This had, in fact, been foreseen. When, in 1943, plans were being prepared for bringing relief food supplies to the people of France, Belgium and the Netherlands, those concerned were brought under heavy pressure to provide enormous supplies of vitamins. It was urged that rickets, scurvy, pellagra and other deficiency diseases were rife and that medication to deal with them was every bit as vital a provision as food to fill bellies. We did not act on that advice. It seemed that an analysis of the evidence justified the belief that the primary problem was to provide calories and that we could safely trust in the wisdom of Bayliss and let the proteins, and at the same time the vitamins, look after themselves; an exception was made, of course, in special provision for children. Events proved that this was the right course to follow.

I suppose I saw as much as anyone of malnutrition and starvation in Europe in 1944-5. With that experience in mind one can be much less pessimistic about the consequences of the current food shortage to-day

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than would otherwise have been the case. The people of Western Europe have recovered in a manner that has astonished those who have closely watched the change. Excluding the aftermath of the surge of tuberculosis that affected France in 1940-41 and the Western Netherlands in 1944-45, there are not any serious consequences of undernourishment detectable to-day among the populations as a whole. This is due, in my opinion, to the fact that the deficiency was primarily one of calories and not of essential nutrients, a lack of which may gravely undermine health. It was otherwise in the Far East, where in so many cases the staple cereal of the restricted diets, particularly those eaten by prisoners in Japanese hands, was white rice. The picture there was in sharp contrast to that seen in the U.K. and the occupied countries of Western Europe. Deficiency disorders, some of which will permanently impair health, were all too common in Asia.

Bread of long-extraction flour and a relatively large consumption of potatoes and other vegetables also played a big part in strengthening our own nutritional position during the war period. Indeed, they did more than strengthen it, they made it secure.

NUTRITION DURING THE 1939-45 WAR

The changed character of the food consumption is shown in table 2.

TABLE 2

	lb. per head per year*			
	Pre-War	1942	1944	1946
Meat	131.7	108.8	114.9	112.7
Oils and Fats	45	40	38.9	34.7
Sugar	109.9	72.1	75.7	79.3
Grain products	209.8	244.9	251.1	236
Potatoes	176	233.7	282.2	293.2
Leafy vegetables	70.1	89.6	87.9	80.4
Tomatoes and citrus fruits	46.3	21	25	32.2
Other vegetables	37.3	30	36.8	35.4
Other fruits	95.2	73.2	68.5	73.3

* "Food consumption levels in the U.K." Cmd. 7203, H.M. Stationery Office, 1947.

This all-over picture analysed in terms of nutrients provides the information given in table 3.

Even if these figures are not applicable to the household or the individual, for they are derived from treatment of the total quantities of food moving into civilian consumption, they clearly show the upward trend towards higher vitamin and mineral provision.

More appropriate data for study, however, are those derived from the Ministry of Food domestic consumption surveys, in which many thousands

of families had their weekly purchases of food and change of stocks carefully recorded and analysed. It is earnestly hoped that this valuable collection of statistical data, unique in scope, will be published in the near future. There is one important reservation to bear in mind in considering these data. They refer only to the food consumed in the home. No allowance is made for meals or snacks eaten elsewhere. That is why the *per capita* calorie figures seem low (2,200-2,300). At the same time, it is not irrelevant to point out that a good snack may contribute 200 calories, a good canteen meal 600-900 calories, and a pint of beer not only 120 calories but, more important, a substantial addition to the riboflavine intake.

TABLE 3

	Requirements	Pre-War	1942	1944	1946
Calories	2550	3000	2880	3010	2890
Protein, gm. .. .	65	79.9	86.9	87.3	90
Fat, gm. (from all sources)	—	130.2	119.4	123.9	111.9
Calcium, mgm. .. .	910	693	838	1038	1037
Iron, mgm. .. .	11.7	12.4	15.6	16.1	17
Vitamin A, I.U. ...	3660	3997	3800	3779	3722
Ascorbic acid*, mgm. ..	57	95.7	97.9	107.1	108.8
Vitamin B ₁ , mgm. ..	1.47	1.21	1.74	2.01	1.86
Riboflavine, mgm. ..	1.2	1.61	1.96	2.09	1.99
Nicotinic acid, mgm. ..	12	13.4	14	16	17.3

* not corrected for cooking losses.

Here, then, are some of the records of the analyses of domestic consumption by "working-class" and "middle-class" families. Both are given in order to show how narrow is the gap between them when measured in terms of essential nutrients. The approximation of these figures is not only a tribute to equality of distribution but it provides a striking contrast to the disparities of consumption, related to purchasing power, revealed by Orr's surveys made in the pre-war period (see table 4).

These figures unquestionably explain why the general state of nutrition did not deteriorate during the war years, but tended steadily to improve. A much larger proportion of the population was better nourished than before the war. That fact cannot be evaded. The vital statistics could not have shown the marked and continued improvement that has been recorded if, as is sometimes rather irresponsibly alleged, the war-time diet undermined the health of the Nation.

A few examples from the figures from the public health statistics show the trend up to 1945; the provisional figures for 1946 indicate further improvement (see table 5, p. 11).

Even the tuberculosis statistics are encouraging, having regard to the evidence, strengthened so greatly by records of the war time in Europe,

TABLE 4
NUTRIENT CONTENT OF FOOD PURCHASE (a) PER HEAD PER DAY
MINISTRY OF FOOD WAR-TIME FOOD SURVEY—AUGUST 1945

	Calories	Protein		Fat gm.	Carbo- hydrate gm.	Calcium mgm.	Iron mgm.	Vit. A I.U.	Thia- min mgm.	Ribo- flavine mgm.	Niacin mgm.	Ascor- bic acid mgm.	Vit. D I.U.
		Total gm.	Animal gm.										
<i>Working-Class Households</i>													
August 1945	2230	73.6	34.5	82.0	300	830	13.0	2607	1.43	1.53	12.71	118	135
July 1945	2267	74.7	34.6	83.7	304	875	12.8	2718	1.47	1.60	12.76	112	127
August 1944	2273	68.1	32.8	88.4	303	801	12.8	2647	1.62	1.67	13.26	114	116
August 1943	2212	70.5	32.0	85.2	292	810	13.2	2671	1.54	1.64	12.82	116	123
<i>Requirements</i>													
(b)													
Full	2350	61.1	(c)	(d)	(d)	873	11.2	4337	1.41	1.98	13.44	66	(c)
Restricted..	2350	61.1	(c)	(d)	(d)	723	8.9	3440	1.12	1.53	10.50	53	(c)
<i>Middle-Class Households</i>													
August 1945	2127	72.6	37.0	80.1	280	896	12.4	2858	1.36	1.64	12.54	107	151
July 1945	2048	69.1	36.3	81.8	260	907	11.6	3097	1.28	1.62	11.34	90	132
August 1944	2258	68.9	36.2	90.2	296	871	12.7	3316	1.55	1.76	13.46	103	133
<i>Requirements</i>													
(b)													
Full	2356	61.2	(c)	(d)	(d)	838	11.3	4538	1.41	2.00	13.63	67	(c)
Restricted..	2356	61.2	(c)	(d)	(d)	663	8.7	3443	1.08	1.49	10.32	52	(c)

(a) Gross purchases include foodstuffs from gardens. (b) Based on all samples surveyed during 1944. (c) Not available. (d) Fat should provide 27-30 per cent. of the total calories of the diet, and carbohydrates not more than 60 per cent.

No allowances are made in the above table for losses of vitamins in cooking which, in the case of ascorbic acid, result in an actual intake substantially lower than the figures shown, perhaps by as much as 70 per cent.

that the incidence of this disease is related to undernourishment. The mortality reached a record low level in 1945, after having shown a transient rise in 1940-41, such as was seen in most of the Western European countries at that time.

No one denies that our food during the war years was dull, unappetizing and monotonous. It was one of the many unpleasant conditions and hard-

TABLE 5

	1936	1939	1945
Maternal mortality (per 1000 births)	3.19	2.55	1.47
Stillbirth rate (per 1000 births)	40	38	28
Neo-natal mortality (per 1000 live births) ..	30	28	25
Infant mortality	59	51	46

ships we had to endure, all of which contributed to make us a very tired people when peace came. Not surprisingly, there was a sharp reaction when the strain of war was eased. Relaxed to some extent, the people realized how tired they had become. All would have been well if they had then begun to enjoy steady amelioration of their lot, but, instead, life became more and more arduous. Surely, it is not a matter for surprise that practitioners report an increase in the numbers of those complaining of being tired, nervy, and in need of a "pick-me-up". But malnourishment is quite another question and I submit that, with the whole range of signs of dietary inadequacy available to assess the nutritional state of the people, no evidence has yet been presented to show that it has declined.

THE FUTURE

The period in the immediate future will be one of great anxiety. I do not believe the calorie requirements will be fully met. Production will be affected directly and also, I believe, indirectly, by an intensification of the psychological reaction to the imposition of further restrictions. There is little that can be done about it. The world food situation is every bit as bad as Sir John Orr and his F.A.O. colleagues insist is the case, although few seem to grasp the grim truth behind their gloomy predictions. Things will probably become worse before they are better. Additional food cuts may be necessary. If they are imposed the lines of the picture which I have drawn will be proportionately broader, but it will remain one essentially reflecting calorie deficiency and little else. In that conclusion there is a gleam of reassurance because the health of the people as determined by their nutritional condition should not be impaired. On the other hand, morale and industrial production will certainly suffer, perhaps to a quite serious extent.

What hope is there that the supply situation will materially improve?

TABLE 4
NUTRIENT CONTENT OF FOOD PURCHASE (a) PER HEAD PER DAY
MINISTRY OF FOOD WAR-TIME FOOD SURVEY—AUGUST 1945

	Calories	Protein		Fat gm.	Carbo- hydrate gm.	Calcium mgm.	Iron mgm.	Vit. A I.U.	Thia- min mgm.	Ribo- flavine mgm.	Niacin mgm.	Ascor- bic acid mgm.	Vit. D I.U.
		Total gm.	Animal gm.										
<i>Working-Class</i> <i>Households</i>													
August 1945	2230	73.6	34.5	82.0	300	830	13.0	2607	1.43	1.53	12.71	118	135
July 1945	2267	74.7	34.6	83.7	304	875	12.8	2718	1.47	1.60	12.76	112	127
August 1944	2273	68.1	32.8	88.4	303	801	12.8	2647	1.62	1.67	13.26	114	116
August 1943	2212	70.5	32.0	85.2	292	810	13.2	2671	1.54	1.64	12.82	116	123
<i>Requirements</i> (b)													
Full	2350	61.1	(c)	(d)	(d)	873	11.2	4337	1.41	1.98	13.44	66	(c)
Restricted..	2350	61.1	(c)	(d)	(d)	723	8.9	3440	1.12	1.53	10.50	53	(c)
<i>Middle-Class</i> <i>Households</i>													
August 1945	2127	72.6	37.0	80.1	280	896	12.4	2858	1.36	1.64	12.54	107	151
July 1945	2048	69.1	36.3	81.8	260	907	11.6	3097	1.28	1.62	11.34	90	132
August 1944	2258	68.9	36.2	90.2	296	871	12.7	3316	1.55	1.76	13.46	103	133
<i>Requirements</i> (b)													
Full	2356	61.2	(c)	(d)	(d)	838	11.3	4538	1.41	2.00	13.63	67	(c)
Restricted..	2356	61.2	(c)	(d)	(d)	663	8.7	3443	1.08	1.49	10.32	52	(c)

(a) Gross purchases include foodstuffs from gardens. (b) Based on all samples surveyed during 1944. (c) Not available. (d) Fat should provide 27-30 per cent. of the total calories of the diet, and carbohydrates not more than 60 per cent.

No allowances are made in the above table for losses of vitamins in cooking which, in the case of ascorbic acid, result in an actual intake substantially lower than the figures shown, perhaps by as much as 70 per cent.

HOW A NUTRITION SURVEY IS CARRIED OUT

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THE sum of weights of nutrients absorbed by consumers is considerably less than the sum of the weights of animal products, fruits and vegetables for human consumption that are produced. At various levels parts are discarded, spoilt or diverted to other uses, and finally small amounts of protein, fat and even carbohydrate are not absorbed. Mottram and Graham (1943) explain very clearly the difference between "intake" (the amounts absorbed) and "input" (amount eaten), and the losses as "plate waste" (amount served but not eaten) and "kitchen waste" (amount bought but not served). These losses have been studied in some detail. So, doubtless, have the amounts discarded, spoilt and diverted in commercial processing and distribution, but these have not been published and the validity of such estimates has not been discussed.

The amounts of food destined for human consumption can be estimated at various levels. The estimate at any of these levels may be the most valuable for a specific purpose. In regulating the supply of food to the country the Ministry of Food must know the amounts imported and produced in the country. In studies of metabolism the physiologist must know the amounts absorbed. As we have seen lately, much confusion may be caused by comparisons between amounts estimated at different levels without realization that none of these estimates is accurate and that the allowances for loss between one level and another are very rough indeed.

(I) *National surveys*.—Estimates of the average amounts of foodstuffs consumed per head can be based on the amounts imported and produced in the country. Such estimates have been published in "Food Consumption Levels" (Ministry of Food, 1945, 1947). The first of these publications explains how these estimates are obtained. During and since the war full records have been kept of the arrivals, stocks, and releases of imported flour, and weekly returns have been made by millers of deliveries of the flour which they mill. Import statistics cover some half of the supply of meat. Since the war the number of slaughter houses in Great Britain has been reduced to 700 and accounts kept of the supplies of meat. The estimates of milk are based on records of sales by the Milk Marketing Board. The estimates of the amounts of these foodstuffs and of butter and sugar are therefore fairly accurate, but the estimate of eggs, poultry and fresh vegetables (based on acreages and estimated yields) must be very rough.

Calculation of the amounts bought by consumers from amounts produced and imported involves assessment of losses, spoilage, and deflection from

If it were possible to obtain wheat in large quantities the position would be greatly improved. That was, of course, a major objective of the resumption of the trade discussions in Moscow. No other comparable supply of calories is available to us, so long as the dollar situation remains as it is to-day. Our renewed agricultural drive will help, but not for at least a year to come. The ill-advised official action of prematurely encouraging home agriculture to revert to livestock and reduce production of grain and potatoes is in no small part responsible for our condition to-day, although the abnormal season of 1947 hit us even harder.

The outlook for the next year, and perhaps for two years, is undoubtedly discouraging, but it is gleaming with hope by comparison with the world food situation. The gap between production and requirements steadily grows. Populations in the Far East and elsewhere are increasing at an incredible rate and will soon provide an insoluble problem, so far as food is concerned. We may live to see world famines of dimensions never before experienced by man. It is hard to believe that it can be otherwise.

There is a long-range solution to the problem. The productive capacity of the tropical belt of Africa and S. America could meet the full needs of mankind for centuries to come. But the mind is numbed by contemplation of the magnitude of the tasks that will have to be engaged: forest clearance, disease eradication, prevention of soil erosion, sanitation, drainage and pest control are only some of the major obstacles to be met. We should at least be proud that our pioneering spirit is still alive and that we have led the way with an enterprise aimed at developing along the most modern scientific lines the production of oil seeds on a vast acreage in Tanganyika that is now virgin forest and scrub. That great experiment may well prove to be the successful small-scale trial that will show the peoples of the world how the formidable problem they must face, and face internationally, can be solved for man's salvation.

(III) *Consumption by individuals*.—A record is kept of all the food eaten. The principal surveys made by this method in Britain have been those of Widdowson and colleagues (1936, 1941, 1942, 1947; McCance *et al.*, 1938). In these the subjects were provided with a balance weighing by $\frac{1}{4}$ oz., a set of instructions and recording forms. The subject weighed and recorded helpings of food, as received, and any edible food left, but not inedible parts. In order to reduce the trouble in weighing Bransby and Wagner (1945) supplied homely measures—cups and spoons—for most foodstuffs and diagrams for measuring such foods as meat; Pyke (1947) used the same method. The estimates obtained in this way are, on the whole, slightly higher than those obtained by actual weighing (Bransby and Wagner, 1945). As it takes much more trouble to weigh all the food eaten by an individual than to keep records of a family's food, the individuals whose diets are studied by this method are still less a random sample of a community than are those studied by method II. But in the survey of Bransby and Wagner (1945), in which the measurements were simplified, few of the families chosen refused to keep records. A fair indication of the type of food eaten by an individual, and a very rough estimation of the amount, can be obtained by asking what foods he ate during the preceding day, or preceding two or three days, with, again, homely measures, diagrams or models for estimating the amounts.

HOW FAR IS THE RECORDED DIET A FAIR SAMPLE?

The food eaten during the period of investigation should be a fair sample of the usual diet of the subjects. The period of investigation should be long enough. As diet commonly has a weekly rhythm a week should be the minimum period; few subjects will tolerate a longer period. The amounts of food vary widely from day to day. The differences from week to week may still be fairly large (Widdowson, 1947), but in a group these weekly variations should, as a rule, balance out. However, the week's sample may not be a fair sample for other reasons. The subjects may wish to show how well or how badly they feed. It can be realized easily that, at the present time when feeling runs high, many persons would more or less unconsciously take special pains or, on the other hand, take less pains than usual to get extra unrationed food.

In the method II(b), prying into the purchase and disposal of food may distort a family's habits. In method III there is, as Grant (1945) points out, a tendency to simplify the diet in order to reduce the trouble of weighing. This is more likely to occur when an individual weighs his own food than it is when a parent weighs the food of a child who is one of a family. Method II(a) measures foodstuffs most accurately; but this advantage is apt to be outweighed by the unrepresentative character of the sample of the population studied and of the diet during the period of investigation.

human consumption. Apparently only spoilage of perishable food has been taken into account in "Food Consumption Levels". Detailed studies of this factor have been made but rarely, and in general more or less arbitrary deductions have been based on general trade experiences. There is therefore a gap between the amounts as estimated in "Food Consumption Levels" and the amounts bought in shops.

(II) *Family surveys*.—The next level at which the supply of food, as a whole, can be considered is at the stage of purchase by the housekeeper. A record is kept of the food eaten by a number of families during a fixed period. The record may be made in one of two ways:—(a) The housekeeper keeps a record, on forms provided, of the amounts of all foodstuffs brought into the house during the period. (b) An investigator weighs and measures all food brought into the house, all stocks of food at the beginning and end of the period, and all waste. The record is kept by the housekeeper in the first method and by the investigator in the second. This is the chief difference between the two methods. The investigator is likely to measure more accurately and is less liable to forget to enter items; although the housekeeper will probably not forget any items if she follows instructions and makes a point of entering all foodstuffs on the record directly they are brought into the house. In method II(a) an investigator may weigh stocks at the beginning and end of the period, but cannot measure waste.

Such surveys are not, as a rule, made in order to estimate what certain individual families eat, but in order to deduce the average amounts eaten by the community or by certain sections of the community. However, it would not be possible to survey even the whole of a section; a sample must be selected for survey. First, the sample must be large enough; this point has not been considered fully but is mentioned by Bransby (1945). In the second place the sample must be representative. Every effort may be made to choose a random sample; for example, every tenth family in a register of residents may be chosen. But the need for the will and ability to keep a record and for the patience involved in keeping it for the whole period excludes certain types—the hostile, stupid, slovenly, lazy and, possibly also when method II(a) is used, the very busy. Some families will object to prying into their private affairs, particularly by method II(b).

The measurement of kitchen and plate waste in method II(b) is intended to bring the survey down to the next level—that of actual consumption. The results obtained by the two methods II(a) and (b) differ by the amounts of "kitchen" and "plate" waste. Thus some 14 per cent. of potatoes are discarded as peel and about half the weight of a cabbage, as bought, consists of outer leaves which are not eaten (Mottram and Radloff, 1937). Such differences must be taken into account when comparing the results of surveys, such as that of the Ministry of Labour (1940) or of Crawford and Broadley (1938), made by method II(a), with others, such as that of Potts (1939) in the West Riding, made by method II(b).

of man, wife and three children requires $(0.8+0.8+1.2+1.0+1.0)$ gm. of calcium per day. If the family's total intake is 3.6 this is 75 per cent. of requirements. Using this method Bransby and Wagner (1945) reckoned that children of Salford and Stoke-on-Trent in 1944-45 were getting 57 to 63 per cent. of their calculated requirements.

FALLACIES IN APPLICATION OF THE RESULTS

Wrong conclusions may be drawn from the results of these surveys unless full account is taken of differences in the methods of survey, the various sources of error associated with these methods and the differences in methods of calculating and presenting the final results.

The results obtained by method I cannot be compared directly with those obtained by methods II(a) or (b). Thus in 1945 the average calories per head according to "Food Consumption Levels" (1947) were 2,940. The food eaten at home by representative working-class families supplied 2,300 calories (about 97 per cent. of requirements according to the standards of the U.S.A. National Research Council), and middle-class families ate less (Drummond, 1946). With full allowance for meals eaten in canteens and restaurants the two estimates differ by at least 340 calories.

The average figure of about 2,900 calories, obtained by method I, is sometimes compared with the number of calories obtainable by a normal consumer in other countries, estimated from the number of calories supplied by his rations and by possible amounts of unrationed foodstuffs (e.g. Fleisch, 1947). But the number of calories obtainable by a normal consumer in Britain, calculated in this way, is not 2,900, but about 2,100.

It appears that Orr (1936) did not base his calculation of the composition of the diets by income groups (Table VII in "Food, Health and Income") on the actual amounts of food eaten by various income groups, as found in surveys, but on figures levelled up in order to agree with estimates of the amounts of food imported and produced in the country. The figures in this table should not therefore be compared with those given by Drummond (1946), but with those given in "Food Consumption Levels" (1945, 1947). Also, in calculation of calories and so on, Orr does not seem to have allowed as much for waste as is now usual.

Calculations in which allowance is not made for losses in cooking may be misleading. Thus in "Food Consumption Levels" (1945) no allowance is made for loss of ascorbic acid in cooking; according to this estimate the amount per head was 112 mgm. in 1934-38, and 127 mgm. in 1943. The amounts in the food actually eaten were considerably less, and the ratio of amount eaten to the estimate was less in 1943 than in 1934-38. For in 1934-38 a considerable proportion of the ascorbic acid was supplied by fruits which were eaten raw or suffered little loss of ascorbic acid in cooking; in 1943 most of the ascorbic acid was supplied by vegetables and some three-quarters was lost in cooking.

Calories and nutrients.—Representative foods are analyzed and the results embodied in food tables. In calculating the calorie values a small allowance is made in the tables for amounts that are not absorbed. The tables may give either (A) the composition of the *edible* portions of foodstuffs or (B) the food value *as purchased*; in (B) allowance is made for inedible parts that are discarded. Thus, according to the Accessory Food Factors Committee (1945) potatoes *as purchased* supply 55 calories per 100 gm., whereas the *edible portion* supplies 73 calories per 100 gm. Samples of diets have been analyzed and the findings compared with the composition as calculated from food tables (Patterson and McHenry, 1941; Young and McHenry, 1942; Widdowson and McCance, 1945). On the whole the agreement has been good, although individual estimates may be as much as 20 per cent. out. But hard water may add appreciable amounts of calcium to cooked food and contamination with iron from knives and cooking utensils may make the calculated amounts of iron entirely misleading (Widdowson and McCance, 1943; Yudkin, 1944). Andross (1946) has drawn attention to waste which method II(b) may not take into account. Thus, in poaching an egg, about 15 per cent. of the protein may be lost by powdering and by solution in the water. Allowance is usually made for loss of ascorbic acid in cooking, but Pyke (1947) found that the actual amounts of ascorbic acid in food as served may be much less than the amount calculated, even with the customary allowance for loss.

No conclusion can be drawn from comparisons of consumption per head in groups of different compositions with regard to sex and age, because the "heads" are not equal. To make such comparisons valid use is made of a statistical device. Each adult man is reckoned as a "consumption unit". Each woman or child is reckoned as one "consumption unit" multiplied by a factor. This unit is often spoken of as an "adult man" and the consumption is reported as so many calories per "adult man"; to avoid confusion it is much better to use the term "consumption unit". The factors, most of which are less than 1, are called family coefficients. According to the scale of coefficients that has been used most widely in Britain (Cathcart and Murray, 1931), a child of five years is reckoned as 0.5 of a unit and a woman as 0.83 of a unit. A family of a man, wife, and three children, aged eleven, nine and five years, would be equivalent to $(1 + 0.83 + 0.9 + 0.7 + 0.5)$ or 3.93 units. If the family consumes 12,183 calories per day, its consumption per unit is 12,183 divided by 3.93 or 3,100, whereas its consumption *per head* is 2,437 calories.

This scale can be used for calories only; for example, children need more calcium than adults. It would be possible to use a scale of coefficients for each nutrient, but the method now most commonly used is to calculate the requirements of a family from tables of requirements, such as those of the National Research Council of the U.S.A., and to express the total intake of a family or a population as a percentage of its requirements. Thus the family

TABLE I

(I)	Significance	Comment
Follicular keratosis or folliculosis	Deficiency of vitamin A	Similar changes caused by deficiency of vitamin C.
Night blindness	Deficiency of vitamin A	Night blindness noticeable only in extreme deficiency.
Impairment of dark adaptation	Deficiency of vitamin A	Estimates unsatisfactory unless final rod threshold measured. Possibly other factors contribute to impairment.
Cheilosis and angular stomatitis	Deficiency of riboflavine	May be due to deficiency of other members of B group.
Corneal vascularization	Deficiency of riboflavine	Not evidence of riboflavine deficiency unless loops of capillaries invade cornea.
Gingivitis	Deficiency of vitamin C	In most cases not related to supply of vitamin C.
Rickets (a) Clinical (b) Radiological (c) Alkaline phosphatase in plasma	Deficiency of vitamin D	Signs on which diagnosis is based should be recorded. Radiologists may disagree considerably among themselves. Range in milder degrees of rickets overlaps normal range. Concentration expressed in Bodansky units is about $\frac{1}{2}$ of those in King-Armstrong units.
Hæmoglobin concentration	Deficiency of iron	Large subjective errors frequent in estimations by methods commonly used.
Serum protein	Deficiency of protein	May be normal on low protein diet and vary inversely with the protein in the diet.
(II) Concentration of vitamin A in plasma	Index of stores of vitamin A	Not significant unless under 40 I.U. per 100 c.cm. Probably affected by other factors besides the supply of vitamin A.
Concentration of carotene in plasma	Index of stores of carotene	Varies rapidly with intake of carotene.
Concentration of ascorbic acid in plasma	Index of recent intake of vitamin C	Responds in a few days to changes in diet. Values of over 3 mgm. per 100 c.cm. show diet is adequate.
Concentration of ascorbic acid in white cell layer of blood	Index of stores of vitamin C	Values below 20 mgm. indicate that stores are adequate.
Ascorbic acid saturation test	Index of stores of vitamin C	The best test but cannot be made on large numbers.

It should be realized that the "adult man" of food surveys is a statistical fiction. Bicknell (1947) states that "the average calorific intake of the unemployed in Newcastle-on-Tyne in 1933, during the dreadful years of unemployment, was 2,837 for men, and for women 2,355", and compares this amount with his estimate of the amount that a "normal consumer" can now get. But the Newcastle survey (no date), which was actually made in 1934, did not measure the amount eaten by any individual man or men, employed or unemployed; the consumption per consumption unit or "adult man" not *per man* was calculated from surveys of the food consumed by groups of families taken as a whole.

ASSESSMENT OF THE STATE OF NUTRITION

Clinical assessment.—Subjects may be classified on the basis of their general appearance into categories—for example, (A) excellent, (B) good, (C) inferior and (D) bad. The results of these classifications, based on subjective impressions, are most unsatisfactory. The standards of different observers may be very different and if an observer examines a group of children on two occasions his two classifications may differ considerably.

Heights and weights.—Schoolchildren are commonly weighed and measured as a routine. These measurements are one of the best indices, as the results should be independent of the observer and can be expressed in figures which should have the same meaning all the world over. Unfortunately children are weighed in varying amounts of clothes. No conclusions can be drawn from comparisons between weights of two groups unless it is known how much clothing the children wore; but quite often the amounts are not specified.

Specific evidence.—Investigators may look for specific evidence of the state of nutrition in respect of certain nutrients (table I). Evidence of this kind is of two types: (i) Evidence of the effects of lack of certain nutrients on the structure or functions of the body. (ii) Estimates of the subjects' stocks of certain vitamins.

The recognition of signs of type (i) is far less a matter of the personality and mood of the observer than is the general clinical assessment of the state of nutrition; for the investigator has to decide whether something that can be defined is or is not present. But it appears that these signs, particularly follicular keratosis (Stannus, 1945), are not as specific as had been supposed. It is questionable whether the level of hæmoglobin varies with the amount of iron in the diet, when this lies within physiological limits.

The results of laboratory tests can be expressed in figures which, like measurements of heights and weights, should mean the same all the world over. Unfortunately they do not. The concentrations of hæmoglobin in the blood are commonly expressed as per cent. of some arbitrary normal and these normals may differ by as much as 20 per cent. Many estimations of

SOME RECENT ADVANCES IN VITAMIN SCIENCE

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THE original historical concept of vitamins has undergone a broadening and deepening with time. The broadening is in part expressed by the extended list of substances that are to-day placed in the category, even though the simplicity of the original definition has perforce long since had to be abandoned. Indeed it has now become impossible even to attempt to define vitamins as a class, for there is no single characteristic, physiological or chemical, that they all share in common. Even the property of essentiality can only be assigned to them in terms of a description that is as full of saving clauses as a good cake is of currants. The bovine and most other mammalian species, with the exception of man, monkey and guinea-pig, and all birds, so far as we know, require no ascorbic acid, yet if ever a substance had a claim on historical and therapeutic grounds to be put into the vitamin category, surely it is vitamin C. The rat and the mouse normally require no nicotinic acid, although there are circumstances in which it is possible to make them exhibit symptoms of its deficiency. It is philosophically sound to regard the term "vitamins" as indicative rather of a manner of investigation in a particular period of the history of medical science than as a class of substances, in the sense in which we speak even of so diverse a group as the alkaloids or the glycosides. The nearest analogy is perhaps the hormones, which range in complexity from relatively simple bases, such as adrenaline, through more complex steroids to the proteins of the anterior pituitary factor or factors. But at least the hormones can be defined in terms of a similar physiological pathway, whereas such a connective link is denied to the "family" of vitamins.

The concept of vitamins has deepened in so far as the last two decades have immensely extended understanding about the part some of them play in cellular metabolism. Although this may not have any very direct bearing on the therapeutics of vitamins and their preventive use against deficiency diseases, all new biochemical and physiological knowledge is at least of this importance to the physician, that it helps to fill in the details of man's normal and pathological make-up, with a concomitant increase of understanding about the etiology of disease and the factors making for health.

ASCORBIC ACID

It is a curious fact that the vitamin first to be isolated pure, to have its constitution established and to be synthesized, that is, ascorbic acid, is still one about which we have no knowledge of its biochemical function. It is sometimes stated, but without any experimental justification, that the part played

serum protein by the Kjeldahl method have been most inaccurate; estimations by other methods, standardized by the Kjeldahl method, have been equally inaccurate. Estimations made by the copper sulphate method using the formula recommended by Phillips *et al.* (1945) are about 6 per cent. lower than those given by accurate Kjeldahl estimation.

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close quantitative study of the relationship between protein and calorie requirements of emaciated or starving human subjects, may find illumination in so apparently remote a place as the inner fastnesses of biochemical laboratories where these complex and subtle enzyme systems are being studied.

It has also recently been shown with considerable probability that the more newly discovered substance, *biotin*, has functions connected with enzyme systems, and other work indicates a rôle for pantothenic acid in the acetylation reactions of cells. It may, perhaps, be pointed out here that the two substances last mentioned, as well as *folic acid*, are to be counted among those vitamins the unmasking of which took place during the war years. As was only to be expected, much of the important work involved was carried out in the United States, but it may legitimately be claimed that British biochemists and nutritionists, even under the stress of war-time conditions, have played a considerable part in the developments. The three compounds in question all form part of that hotch-potch commonly called "the vitamin B₂ complex": each has had its constitution precisely determined, each has been synthesized and each has been prepared on a manufacturing scale, or can be when the demand warrants it. Biotin deficiency can certainly be produced, and may possibly occur spontaneously, in human subjects, although knowledge of its physiology and pathology has been mainly derived from studies on rats and chickens.

There is no need to write here of the dramatic results obtained with *folic acid* when this is used in the treatment of pernicious anæmia and other blood dyscrasias, provided the warning be added that, at any rate so far, it has not been found capable of dealing with the neurological complications of Addisonian anæmia. The importance of folic acid to those concerned with the etiology of this disease lies, paradoxically enough, in the fact that it is certainly not identical with the anti-anæmic factor of liver, so that any explanation of the hæmatological abnormalities present must be able to account for both the similar and the different effects of folic acid, a very unusual form of dipeptide, of its "conjugates" which are glutamic acid polypeptides of folic acid, and the anti-anæmic factor itself, which has entirely different structure and is active at very much lower doses.

Of *pantothenic acid* in human metabolism nothing is known, except for the interesting suggestion, coming from the medical officer at a prisoner-of-war camp, that its deficiency may be the cause of the burning foot syndrome frequently seen in these camps. This work awaits confirmation and extension.

Among the other members of the afore-mentioned "vitamin B₂ complex" are several of which it can legitimately be said that they are almost certainly essential to man because of their widespread and almost universal occurrence in the cells of plants and animals of innumerable species and of various degrees of complexity or integration. Included in these can be reckoned choline—probably the bodily precursor of acetylcholine—inositol, a hexahydric alcohol, and *para*-aminobenzoic acid, which is almost certainly closely

by this substance in the cell is associated with the fact that it is an oxidation-reduction catalyst. It is well known that ascorbic acid can be oxidized under appropriately mild conditions to, and appears in both vegetable and animal cells as, dehydroascorbic acid, a substance having the same antiscorbutic activity as vitamin C and capable of reversible reduction to its parent substance. Such a system looks as if it might take part in the transport of hydrogen during the oxidative breakdown of carbohydrate or other metabolites. Yet there is not a scrap of experimental evidence to show that ascorbic acid acts thus. Any statements to that effect found in the literature or in "medical" propaganda must be regarded as an expression of opinion and not as a condensed statement of verified fact.

THE VITAMIN B COMPLEX

It has long been known that certain water-soluble vitamins, sometimes associated with the phosphate radicle and sometimes without it, often combined also with adenine and ribose to form nucleotides, are attached loosely to certain highly specific proteins (the apo-enzymes) to form the whole catalytic system (holo-enzyme) of which they constitute an essential part (the co-enzyme). The function of *vitamin B₁* (aneurine in this country, thiamin in the United States) in the form of its pyrophosphate, to act as co-enzyme for the system that catalyses the breakdown of pyruvic and lactic acids during the later stages of glucose degradation in the animal or vegetable cell, is now so well known that its demonstration is already regarded as a piece of classical biochemistry. Hardly more recent is the understanding of the parts played by certain members of the *vitamin B₂* complex, specifically riboflavine and nicotinic acid, as prosthetic groups or co-enzymes for other systems necessary to those chain-like processes of energy liberation within the cell that are, perhaps, the most characteristic reactions of living matter. It has been said that the essence of life is the burning of carbohydrate so slowly as to result in maximum liberation of energy and minimum thermal damage to the tissue involved. In this process, the enzymes, including those of which the co-enzymes contain vitamins in their molecules, play an essential part.

Further work has increased the number of vitamins of which it can now be said with certainty that at least one of their rôles is connected with enzyme activity. It is fairly recently that *vitamin B₆* (formerly called "adermin") has been found to consist of three different closely related substances, pyridoxine (the first to be identified), pyridoxal, and pyridoxamine. It has now been shown that the aldehyde form, pyridoxal, as its phosphate, is the co-enzyme in systems involved in certain stages of the breakdown of amino-acids, specifically transamination and decarboxylation. The former is a bridge between protein and carbohydrate metabolism, for an amino-acid after transamination becomes a keto-acid and can then take its place amongst the metabolites involved in carbohydrate breakdown. It is not unlikely that some of the work carried out in Western Europe after VE-Day, involving

close quantitative study of the relationship between protein and calorie requirements of emaciated or starving human subjects, may find illumination in so apparently remote a place as the inner fastnesses of biochemical laboratories where these complex and subtle enzyme systems are being studied.

It has also recently been shown with considerable probability that the more newly discovered substance, *biotin*, has functions connected with enzyme systems, and other work indicates a rôle for pantothenic acid in the acetylation reactions of cells. It may, perhaps, be pointed out here that the two substances last mentioned, as well as *folic acid*, are to be counted among those vitamins the unmasking of which took place during the war years. As was only to be expected, much of the important work involved was carried out in the United States, but it may legitimately be claimed that British biochemists and nutritionists, even under the stress of war-time conditions, have played a considerable part in the developments. The three compounds in question all form part of that hotch-potch commonly called "the vitamin B₂ complex": each has had its constitution precisely determined, each has been synthesized and each has been prepared on a manufacturing scale, or can be when the demand warrants it. Biotin deficiency can certainly be produced, and may possibly occur spontaneously, in human subjects, although knowledge of its physiology and pathology has been mainly derived from studies on rats and chickens.

There is no need to write here of the dramatic results obtained with *folic acid* when this is used in the treatment of pernicious anæmia and other blood dyscrasias, provided the warning be added that, at any rate so far, it has not been found capable of dealing with the neurological complications of Addisonian anæmia. The importance of folic acid to those concerned with the etiology of this disease lies, paradoxically enough, in the fact that it is certainly not identical with the anti-anæmic factor of liver, so that any explanation of the hæmatological abnormalities present must be able to account for both the similar and the different effects of folic acid, a very unusual form of dipeptide, of its "conjugates" which are glutamic acid polypeptides of folic acid, and the anti-anæmic factor itself, which has entirely different structure and is active at very much lower doses.

Of *pantothenic acid* in human metabolism nothing is known, except for the interesting suggestion, coming from the medical officer at a prisoner-of-war camp, that its deficiency may be the cause of the burning foot syndrome frequently seen in these camps. This work awaits confirmation and extension.

Among the other members of the afore-mentioned "vitamin B₂ complex" are several of which it can legitimately be said that they are almost certainly essential to man because of their widespread and almost universal occurrence in the cells of plants and animals of innumerable species and of various degrees of complexity or integration. Included in these can be reckoned choline—probably the bodily precursor of acetylcholine—inositol, a hexahydric alcohol, and *para*-aminobenzoic acid, which is almost certainly closely

involved in those stages of bacterial metabolism that are disturbed or terminated in the presence of sulphonamides.

VITAMIN SYMBIOSIS

The last observation may serve as a convenient link with another aspect of vitamins that has assumed rapidly increasing importance, at any rate to the laboratory worker, and so, indirectly and ultimately, to the practising physician, during the last few years. It has happened more than once that the study of bacterial metabolism has given vital clues in the field of human nutrition. The discovery of biotin, one of Wildier's original "bios" components, arose from investigations into the factors necessary for yeast growth. It only gradually became evident that it was identical with the substance capable of combating egg-white poisoning which had been produced in rats by workers in an entirely different field of study. The explanation involved by the discovery of the curious protein, avidin, present in raw egg-white and destroyed by cooking, which could "bind" and immobilize biotin, led to a search for other "anti-vitamins", and this field of investigation is still being actively tilled. It is necessary, apparently, to distinguish between three types of anti-vitamin action: first, there may be temporary or permanent immobilization of a vitamin, as in the avidin-biotin instance; secondly, there are certain enzymes directly destructive of particular vitamins, a case in point being the vitamin B₁-destroying substance "thiaminase" in certain fresh water fish, which irreversibly inactivates aneurine much as penicillinase destroys penicillin; thirdly, there are more physiological antagonists which work by jumping the claims of vitamins in intracellular enzyme systems, although they are chemically unable to indulge in any productive operations on the territory so acquired!

Not only have considerations of this kind and a vast amount of intricate and fascinating experimental work been derived quite unexpectedly from work in the field of bacterial metabolism, but there have been two separate developments, distinct from each other, both of very great practical importance. The first of these involves the use of bacteria as reagents for the quantitative measurement of certain vitamins. The study of bacterial metabolism, in particular attempts to devise suitable wholly synthetic media for the growth of micro-organisms, has led to detailed knowledge of the nutrient requirements, at any rate of some.

By inoculating with a suitable organism a medium complete in everything except one vitamin nutrient, and then adding graded quantities of the missing vitamin to different inocula, a graded response in bacterial growth can be obtained and this may be measured by turbidometric or other procedures, including straightforward titration of the acid formed if the organism belongs to the *Lactobacillus* or other suitable group.

The use of this analytical technique has made it possible to investigate not only a wide range of substances, but, what is becoming to the nutritionist increasingly important, a wide range of samples of ostensibly the same food for their contents of certain vitamins about whose *range* of concentrations

knowledge has hitherto been almost non-existent. It may confidently be forecast that tables of food analyses will soon begin to show the results of the extensive microbiological assays being carried out in various parts of the world.

The same procedure is applicable to the determination of most, if not all, of the nutritionally essential amino-acids, after their liberation from proteins by suitable methods of hydrolysis. By that same token, tables of food composition in future should be able to give more and more information about the amino-acid composition of foods, instead of about a hypothetical "protein content", which is merely the result of multiplying a "Kjeldahl nitrogen" figure by an empirical factor.

In the course of studying bacterial metabolism it has become abundantly clear that there is an enormous range of difference between the nutritional requirements of different micro-organisms.

Some are extremely exacting and can only be grown on media so complex that it has not in point of fact been possible to compound them entirely out of known chemical substances. Others can be grown on relatively simple mixtures of pure carbohydrate and salts, sometimes with the addition of one or two of the known vitamins in pure form. Organisms of the latter group are found in many instances to have supplied their metabolite liquid with considerable quantities of vitamins not originally present in it. These substances must clearly have been synthesized by the organism.

The question immediately arises, do such syntheses take place *in vivo* as well as *in vitro*? To this to-day the answer is unequivocally "Yes".

It has been shown not only in experimental animals, and particularly in the rat and the mouse, but also in human volunteers, that aneurine, nicotinic acid and riboflavine at least, and almost certainly other water-soluble vitamins, as well as vitamin K, are synthesized by the normal flora of the intestinal tract in quantities that make a significant contribution to daily intake. Sterilization of the gut by means of one or other of the less soluble sulphonamides may lead to a rapid fall in, and even to complete cessation of excretion of one or more of these vitamins. It is clear that the lower intestine of non-ruminants plays a part analogous with that of the bovine rumen. For years the cow has been envied for her ability to make use of cellulose and other carbohydrate foods unavailable to man. It is now known that the credit should lie with the vegetable rather than the animal kingdom and that the micro-flora (and possibly also the micro-fauna) of the cow's alimentary tract are the effective agents, and not the host organism. In a similar way it must be recognized that man's alimentary allotment can supplement the produce of his kitchen garden.

Therapeutic implications.—There is no space here to follow in detail the many interesting inferences that may be made from our present clear proof of this latest example of symbiosis. Amongst them may be mentioned the fact that withdrawing one vitamin from an animal's diet may cause manifestations of the deficiency of a different vitamin. This can be explained on the basis of the essentiality of the first vitamin to some group of alimentary micro-organisms that were supplying the host with its requirements of the second. The concept has also helped to throw light on the great pellagra

paradox, that is, to explain how foods of apparently identical nicotinic acid content could be widely different in their pellagragenic activity. Apart from the possible presence of certain anti-nicotinic acid substances—and there can be no doubt whatever about the specificity of pure synthetic nicotinic acid in dealing with the major pathological lesions of pellagra—it would appear that the micro-flora producing significant quantities of nicotinic acid in the human gut are somewhat selective. Give them the right diet and they will do their supplementing job; without it they strike and nicotinic acid deficiency results. Furthermore, there is now no doubt as to an intimate connexion—at any rate for certain species of laboratory animals—between tryptophane and nicotinic acid requirements, the amino-acid and the vitamin being to some degree and in certain circumstances interchangeable. This may also be still another relationship involving the intervention of the alimentary micro-flora or indicating an association of the two compounds in their intermediary metabolism. To complicate matters further, it now appears that the conversion of tryptophane to nicotinic acid (or amide) is affected by the amount of vitamin B₆ (pyridoxine) available to the animal. Again, it is not yet clear to what extent these relationships apply to man and therefore whether tryptophane or pyridoxine deficiencies play any part in the etiology of human pellagra.

The interaction of different vitamins may often be of a more direct kind than this. It is now accepted in the treatment of deficiency diseases, especially those occurring among the poorer populations in tropical or semi-tropical countries, that administration of a single pure vitamin for the treatment of a specific condition, such as beri-beri or pellagra, is fraught with the danger of “unmasking” some other latent vitamin deficiency and precipitating an acute manifestation of their symptoms. For this reason a condition of angular stomatitis and cheilosis, recognized as due to riboflavine deficiency, and perhaps confirmed by slit-lamp examination of the eye, should not be treated with high therapeutic doses of riboflavine unless attention is at the same time given to raising the intake of all other known and unknown essential dietary factors by close attention to generally improved nutrition, including supplementation with foods like yeast and liver. These considerations, suitably modified, may well play their part in a reform of hospital diets apparently very much overdue in some places.

OTHER NOTABLE ADVANCES

There remains but little space in which to mention briefly certain other notable advances of the last decade. It would be quite unjustified not to refer to the publication in January, 1943, by the National Research Council (U.S.A.) of their “Recommended Dietary Allowances”, which, despite everything that may have been said by way of criticism and amendment, have, especially with the new amendments included in the revised 1945 edition, been increasingly adopted all over the world as targets for optimal

nutrition. True there has been much misunderstanding, most of it unintentional, but some of it, one cannot help feeling, a little disingenuous, of the purposes for which these allowances were drawn up and the considerations that led to the published figures, and all too frequently they are described as "requirements", which they were never intended to be. One ventures to hope that F.A.O. or W.H.O. will soon publish an equally authoritative set of recommendations that may be available in every country in the world, without the need to write for a copy to Washington and to ask an American friend to pay for it!

The laboratory *synthesis of vitamin A*, recently carried out unequivocally by two Dutch industrial chemists, should be regarded as one of the major academic achievements in the field of vitamin synthesis. It must, however, be emphasized that this success does not necessarily herald the appearance of synthetic vitamin A on the market as the result of large-scale factory operations. With the history of vitamin B₁ synthesis in mind, however, one hesitates to prophesy about such matters, and it is quite impossible to foretell whether shortage of raw material, poor yields or extreme "touchiness" of some of the chemical reactions involved may or may not prove permanent obstacles to commercial manufacture—in other words, whether vitamin A will, from this point of view, fall into the same class as aneurine or as penicillin.

The use of *high doses of artificial vitamin D* (calciferol, vitamin D₂) had, until recent years, been confined in this country to the treatment and maintenance of parathyroprivea cases. Subjects have been kept in normal calcium-phosphorus balance for many years, with no impairment of working capacity, simply by taking at suitable and controlled intervals the necessary high dose. High doses had also been used, both orally and by injection, in the "stosstherapie" of rickets. It was nevertheless with considerable scepticism that the world of medical science first read the report that high doses of calciferol could be used in *the treatment of lupus*. A few lone voices have been crying for twenty years in the vitamin wilderness, asserting that the use of vitamins need not necessarily be confined to the prevention or treatment of deficiency diseases, and that substances of such high physiological activity as, for example, vitamin D itself, or vitamin A, or, as might now be added, biotin, might well be expected in hyper-physiological doses to have a pharmacology of their own—and possibly, as a consequence, a therapy of their own. But the conservative view expressed in the obiter of a nutritionist with world-wide reputation that "the only use for ascorbic acid is for treating scurvy" had till then prevailed. It is going to be difficult for those who adopt this austere attitude to argue that lupus is a form of rickets. Once they admit that it is not, it would seem that the whole of their case disappears and that the possibility of a widely extended therapeutic use for the various vitamins now available in pure form must again be seriously considered both by laboratory worker and by practising physician.

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women and children, the food consumed at home amounts to 2,100 to 2,300 calories with 70 to 80 gm. protein, about half of which is of animal origin. The estimate does not include school meals and milk, canteen and restaurant meals and other supplies obtained out of the home. This means that when allowance is made for the smaller requirements of young children, the adult can get protein well in excess of the "optimal" requirement of 1 gm. per kgm. Pregnant and lactating women, thanks to the "green book", can obtain additional milk, meat, eggs and cheese which take care of their special needs. In families where the children are adolescent, it may be difficult to provide protein commensurate with needs. Similarly, if it is argued that the preferential consumption of very high protein diets by athletes is of physiological significance, heavy workers may be receiving less protein than they require. But it must be stressed that additional provision has been made for these doubtful categories and that they do not seem to be making full use of supplies available to them.

THE NUTRITIVE VALUE OF PROTEINS

It has been accepted for about forty years that the nutritive value of any protein depends upon its amino-acid composition, and that different proteins contain different proportions of the various amino-acids. Woolley (1945) has now shown that amino-acids are not the whole story, at least for rats and certain bacteria, in that a protein derivative of peptide-like structure—strepogenin—is also necessary for optimal growth. It is too early to say what significance this finding has for man.

Until recently there was a lull in amino-acid research, owing to difficulties of technique, but many attempts were made to allot "biological values" to different proteins on the basis of their ability to promote growth or maintain nitrogen equilibrium. Such work was usually carried out on animals with isolated pure proteins and had little relation to ordinary dietary habits. It had, however, some repercussions in medical thought, because out of the early animal experiments arose the custom of arbitrarily dividing proteins into first- and second-class varieties, loosely identified with animal and vegetable protein, respectively. Such a classification has little or no meaning in terms of the proteins of a mixed dietary. Kestner (1947) has demonstrated in rats that although the proteins of bread and potatoes separately have low biological values, when combined in a diet they promote growth as well as meat proteins.

The amino-acids of different proteins in a mixed dietary have the power of supplementing each other, so that the nutritive value of a protein mixture is that of its combined amino-acid structure and is not limited by that of any one protein. Of the twenty-six natural amino-acids so far identified, ten are now known to be essential dietary constituents for the rat—arginine, histidine, lysine, tryptophane, phenylalanine, methionine, threonine, leucine, isoleucine and valine. Subsequent work indicates that this list is equally

PROTEINS AND AMINO-ACIDS IN HEALTH AND DISEASE

By ANGUS M. THOMSON, B.Sc., M.B., CH.B.

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GIVEN a free choice of diet, the average man consumes about 12 per cent. of his calories in the form of protein. That is to say, a 3000 calorie diet tends to contain about 90 gm. protein, or a 4000 calorie diet about 120 gm. Most athletes in training prefer to consume a higher proportion of protein, especially from foods of animal origin. On the other hand, the diet of breast-fed babies provides only 8 per cent. of the calories as protein, although the infantile protein requirement is high relative to that of adults (Cuthbertson, 1940, 1946).

The determination of the minimum and the optimum protein requirement is a problem which has defied satisfactory solution, although a great deal of research has been carried out. Semi-starvation on a low-protein diet causes œdema in man and animals, but the appearance of œdema seems to be a complex phenomenon not associated with a constant threshold level of protein intake. Œdema can appear over a wide range of serum protein levels, including those which are considered to be within the limits of normality (Keys *et al.*, 1946). The determination of the minimum protein requirement has therefore resolved itself into finding the lowest levels at which excretion does not exceed intake. Such investigations have always given results much lower than the levels of intake usual in a "free-choice" dietary, and it seems quite possible to carry on a normal healthy existence on a diet containing not more than 50 gm. of protein daily (Hegsted *et al.*, 1946).

No method of determining the optimal allowance of protein has been discovered, but most authorities agree that adults using a mixed diet of Western type should consume about 1 gm. per kgm. body weight. Infants and young children should receive about three times as much, and older children, adolescents and pregnant and nursing women about twice as much.

Leitch (1942) has pointed out that the percentage of calories derived from protein in most common foodstuffs exceeds 12, thus: wheat flour, 13 per cent.; milk, 21; cheese, 28; potatoes, 10; dried peas and beans, 26; citrus fruits, 8 to 13; leafy vegetables, 13 to 35; bacon, 7; lean meat, 15; white fish, 95; and eggs, 32 per cent. Fat and sugar contain no protein, and if the intake of these items is restricted, as it is under rationing, it is extremely difficult to devise a diet in which the proportion of calories derived from protein does not exceed 12 per cent. Therefore a diet of 2,400 calories almost inevitably contains more than 70 gm. protein. In fact, a normal consumer should not find undue difficulty in obtaining 2,500 calories with 100 gm. protein from his rations and points foods, together with available unrationed foods. It is reckoned that, per head of the population including men,

proteins, and particularly the sulphur-containing amino-acids methionine and cystine, may play an important part in preserving the normal function and structure of the liver. First, fatty liver resulting from choline deficiency can be prevented by feeding certain proteins or methionine. Cystine has an opposite effect, producing a further accumulation of fat in the livers of animals on a fatty diet. Prolonged fatty liver may be followed by portal cirrhosis. Secondly, methionine and cystine have a protective effect against the hepatic lesions caused by certain poisons, such as chloroform. Thirdly, a number of workers have reported the occurrence of massive acute hepatic necrosis of the liver in animals on diets deficient in the sulphur-containing amino-acids. Glynn (1947) has reviewed the evidence.

Much of this animal work is obscure in detail, but the information so far available is of obvious clinical interest. A number of reports have appeared on the effect of methionine, amino-acid mixtures or high protein diets in human hepatic cirrhosis, toxic hepatic disease, and infective hepatitis. It is fair to conclude that a high-protein diet is sound nutritional therapy in dealing with patients with liver disease. I have not been able to conclude that a case has yet been made out for treatment with isolated amino-acids in addition, in any of the conditions so far studied.

From the preventive aspect, there is some evidence that the habitual consumption of a generally poor and monotonous diet with a low protein content is associated with a predisposition to liver disease. Although the incidence of infective hepatitis is not higher in undernourished communities, the case mortality is raised. Trowell (1946) considers liver disease to be one of the chief manifestations of malnutrition in East Africans. These people often have a large liver and develop hepatitis very easily; cirrhosis is very common, and primary liver carcinoma is the most common type of cancer in many parts of their country.

PROTEIN DEPLETION IN DISEASE AND INJURY

Cuthbertson (1946, 1947) has defined the following causes of protein depletion following moderate to severe injury:—(1) Loss of actual tissue; (2) loss of blood or exudate from the damaged area; (3) loss due to excessive breakdown of body protein and excretion of nitrogen; (4) loss due to infection, if that be superimposed; (5) disuse or reflex atrophy.

Protein depletion, from one or more of the above causes, may follow fractures, burns, infarctions, surgical operations and various infections, with or without fever. The losses may be very great. About 850 gm., or about 8 per cent. of the total body protein, may be lost in the ten days following a fracture of the leg, and more than twice this loss may follow a third degree burn involving 60 per cent. of the body surface. Howard *et al.* (1944a) found the average loss in cases of leg fracture to be 1,400 gm. of protein, which is equivalent to about 15 lb. of protein tissue. Similarly large losses occur in fevers, such as typhoid and malaria.

The most important cause of protein loss in such cases is excessive break-

applicable to man, although the exact status of histidine is still in doubt.

An amino-acid is "essential" in the diet if it cannot be synthesized in the body rapidly enough for normal growth and function. The remaining "non-essential" amino-acids are not necessarily completely dispensable, so far as the diet is concerned. It is known that cystine is essential to normal metabolism, but can be formed from methionine if adequate amounts of the latter are in the diet. Conversely, dietary cystine can "spare" methionine. A similar relationship holds between tyrosine and phenylalanine.

The development of new chemical, physical and microbiological methods of estimating the amino-acids in foods means that before long it will be possible to make a fairly accurate analysis of the essential amino-acid content of any diet. Already Block and Mitchell (1946) and others have published tables from which tentative analyses can be made. We have practically no knowledge of human amino-acid requirements in quantitative terms, because no clear-cut deficiency symptoms have been identified, and it is extremely expensive to replace the protein in human diets with pure amino-acid mixtures. The best approach that can be made at present to estimating the nutritive value of a protein mixture is to compare its amino-acid structure with that of a protein which is known to permit optimal growth and function. Whole-egg protein is a suitable standard, and Block and Mitchell (1946) describe a method of calculating the comparative nutritive value of other proteins in terms of the amino-acid in greatest deficit relative to the content in whole-egg protein. This method is still in the research stage but promises well, and it may soon be possible for clinicians to calculate the amino-acid composition of the proteins of any given diet, and to compare their combined nutritive value with that of a chosen standard. In due course it should become possible to deal with each amino-acid separately in terms of need and intake, and then the determination of protein requirements will have been placed on a rational basis. Woolley's work on the peptide streptogenin raises further intriguing possibilities and extensions.

Meanwhile, a few facts are of clinical interest. A comparison of the chief animal and vegetable proteins shows that the latter usually have a lower content of lysine and methionine. In leafy vegetable and pulse proteins the relative lysine deficiency is slight. The relative methionine deficiency in unrefined cereals is not invariable; for example, human milk protein contains less methionine than does whole wheat protein. There is therefore no characteristic difference between the amino-acid content of animal and of vegetable proteins. Few vegetarian diets exclude milk and milk products, and the biological values of milk and of meat proteins are almost identical. The tendency to anæmia associated with vegetarianism (Taylor and Chhuttani, 1945; Marriott, 1945) has probably nothing to do with a difference between animal and vegetable proteins.

PROTEIN AND LIVER DISEASE

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proteins, and particularly the sulphur-containing amino-acids methionine and cystine, may play an important part in preserving the normal function and structure of the liver. First, fatty liver resulting from choline deficiency can be prevented by feeding certain proteins or methionine. Cystine has an opposite effect, producing a further accumulation of fat in the livers of animals on a fatty diet. Prolonged fatty liver may be followed by portal cirrhosis. Secondly, methionine and cystine have a protective effect against the hepatic lesions caused by certain poisons, such as chloroform. Thirdly, a number of workers have reported the occurrence of massive acute hepatic necrosis of the liver in animals on diets deficient in the sulphur-containing amino-acids. Glynn (1947) has reviewed the evidence.

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applicable to man, although the exact status of histidine is still in doubt.

An amino-acid is "essential" in the diet if it cannot be synthesized in the body rapidly enough for normal growth and function. The remaining "non-essential" amino-acids are not necessarily completely dispensable, so far as the diet is concerned. It is known that cystine is essential to normal metabolism, but can be formed from methionine if adequate amounts of the latter are in the diet. Conversely, dietary cystine can "spare" methionine. A similar relationship holds between tyrosine and phenylalanine.

The development of new chemical, physical and microbiological methods of estimating the amino-acids in foods means that before long it will be possible to make a fairly accurate analysis of the essential amino-acid content of any diet. Already Block and Mitchell (1946) and others have published tables from which tentative analyses can be made. We have practically no knowledge of human amino-acid requirements in quantitative terms, because no clear-cut deficiency symptoms have been identified, and it is extremely expensive to replace the protein in human diets with pure amino-acid mixtures. The best approach that can be made at present to estimating the nutritive value of a protein mixture is to compare its amino-acid structure with that of a protein which is known to permit optimal growth and function. Whole-egg protein is a suitable standard, and Block and Mitchell (1946) describe a method of calculating the comparative nutritive value of other proteins in terms of the amino-acid in greatest deficit relative to the content in whole-egg protein. This method is still in the research stage but promises well, and it may soon be possible for clinicians to calculate the amino-acid composition of the proteins of any given diet, and to compare their combined nutritive value with that of a chosen standard. In due course it should become possible to deal with each amino-acid separately in terms of need and intake, and then the determination of protein requirements will have been placed on a rational basis. Woolley's work on the peptide streptogenin raises further intriguing possibilities and extensions.

Meanwhile, a few facts are of clinical interest. A comparison of the chief animal and vegetable proteins shows that the latter usually have a lower content of lysine and methionine. In leafy vegetable and pulse proteins the relative lysine deficiency is slight. The relative methionine deficiency in unrefined cereals is not invariable; for example, human milk protein contains less methionine than does whole wheat protein. There is therefore no characteristic difference between the amino-acid content of animal and of vegetable proteins. Few vegetarian diets exclude milk and milk products, and the biological values of milk and of meat proteins are almost identical. The tendency to anæmia associated with vegetarianism (Taylor and Chhuttani, 1945; Marriott, 1945) has probably nothing to do with a difference between animal and vegetable proteins.

PROTEIN AND LIVER DISEASE

There is now a considerable amount of work on animals which shows that

The following quantities provide roughly 10 gm. of protein:—

Beefsteak, stewed	1½ ounces (43 gm.)
Corned beef	1½ ounces (43 gm.)
Filleted fish	2 ounces (57 gm.)
Cheese	1½ ounces (43 gm.)
Eggs	1½ eggs
Bread	4 ounces (114 gm.)

It is doubtful if one source of a protein is better than another unless from the point of view of palatability. The aim should be a varied, ample and attractive diet. Patients eat food, and care nothing for protein.

Prescribing a diet is one thing, and making sure the patient eats it is another. The subject of hospital diets has been widely discussed in recent years and most authorities seem to agree that the food provided for patients usually suffers from most of the faults traditionally associated with institutional cooking. In how many hospitals do patients not consider it the duty of friends and relatives to supplement the official diet with eggs, fruit, jam, and so on? And in how many is tempting the fickle appetite of an early convalescent patient dealt with by the medical staff as an important aspect of treatment? Where dietary surveys have been carried out in hospitals, the results are not reassuring. Lyall (1945) gives the following average daily intakes in three hospitals:—

	Calories	Protein
General Hospital	1,680	65 gm.
Maternity Hospital	1,840	66 gm.
Hospital for chronic diseases		
Females	1,940	62 gm.
Males	2,150	60 gm.

Such figures are not atypical, and it is evident that patients on such diets receive little nutritional help towards convalescence.

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down of body protein. This curious reaction to any major assault on the tissues has been much studied, both in man and in animals, but its essential nature remains in doubt. Cuthbertson (1946) suggested that it is a reflex designed to mobilize materials necessary for the healing process. The importance to a sick or injured wild animal of even a wasteful means of accelerating recovery is evident, and it is noteworthy that the catabolic reaction is absent when protein reserves have been depleted by previous poor feeding, or by bleeding or other forms of loss. Croft and Peters (1945), having shown that the negative nitrogen balance in burned rats could be greatly reduced by including 1 per cent. of methionine in the diet or by doubling the protein (casein) intake, made the interesting suggestion that the protein loss might be the result of a raid on the tissues for one key amino-acid. This experiment with methionine has been repeated by Peters but with a negative result. Preliminary experiments on men do not suggest that methionine helps to reduce the negative nitrogen balance following burns or trauma. Whatever its explanation, the nitrogen depletion of the body is general, and is not the result of local tissue destruction. Protein catabolism reaches a maximum about a week after injury or the height of a fever, then slowly declines for several weeks, and is succeeded by a phase of anabolism.

It seems almost impossible to establish nitrogen equilibrium by forced feeding at the height of the catabolic phase. Forced feeding may be necessary to overcome the marked anorexia which is usual at this time, and there is no evidence that the infliction of this discomfort on an acutely ill patient is beneficial (Howard, 1944b). But a week or ten days after the injury the catabolic phase goes into decline, and its abolition can be greatly accelerated by giving a liberal high-protein diet. Replenishment of the depleted protein reserves can be expected to hasten convalescence by restoring lost weight and by improving the vitality of the tissues. Residual anorexia can usually be overcome by well-chosen and well-prepared food, and by administering it frequently in small amounts.

In convalescence, the aim should be to attain a daily protein intake of not less than 100 gm., together with sufficient calories to ensure that protein is not expended unnecessarily to provide energy. The Canadian Army investigators recommend a basic hospital diet of 2,700 calories with 100 gm. of protein, served as three meals a day (Stevenson and Bensley, 1947). When considerable weight has been lost, protein supplements should be prescribed, until the total intake reaches 3,200 to 3,800 calories, with 130 to 170 gm. protein. Taylor (1944) recommends 2 to 3 gm. protein and 60 calories per kgm. body weight. Supplements should be given between meals.

Milk and skim milk powder mixtures form the most suitable basis for supplementary protein feeding. A drink based on half a pint of fresh milk and 1½ ounces of skim milk powder provides about 25 gm. protein and 240 calories. Such drinks may be flavoured as desired, and may be diluted if they prove too rich. Other protein-rich foods may be useful for supplements.

infant by drawing on stored reserves. The superior reproductive efficiency of social classes I and II is due to the fact that they have a higher standard of hygiene and education from birth; they have better food, more leisure, fresh air and sleep. During pregnancy they show more initiative in finding out what to do and what not to do and are more conscientious in carrying out the instructions of their medical attendant.

LESSONS TO BE LEARNT FROM ANIMAL EXPERIMENTS

Although the results obtained by animal experiments cannot be applied to the human without caution, they nevertheless repay careful study.

Wallace (1946) has shown that the diet in the last third of pregnancy is most important. Working with sheep he showed that in a group fed badly during the first two-thirds of gestation and then fed on a good diet, the lambs were little inferior to those from sheep well fed during the whole pregnancy. By contrast, when the sheep were well fed during the first two-thirds of gestation and then badly fed up to term the lambs were small and weak. The greatest difference was seen in twin pregnancy. Thomson (unpublished data), working at the Rowett Institute, Aberdeen, reports a fetal mortality of about 80 per cent. in twin lambs of sheep on a low plane of nutrition. Wallace found that when the sheep were fed throughout the pregnancy on a poor diet which caused them to lose 22 lb. (9.99 kgm.) in weight, the lambs weighed on the average 5.8 lb. (2.63 kgm.), whereas when the sheep were fed throughout on a good diet so that they gained over 60 lb. (27.24 kgm.), the birth weight of the lamb was 11.3 lb. (5.13 kgm.). Such extremes of diet and weight gain and loss are unlikely in human reproduction. It would be interesting in due course to know something of the reproductive efficiency of the "low plane" lambs.

All the potentialities of development are already determined at fertilization by the genes, but the pattern of growth and differentiation is laid down and controlled by "organizer substances". These are primary and secondary. The primary have absolute power to determine what a particular part of the dividing ovum shall become. The secondary organizers exercise a decisive effect on differentiation at a particular stage and later may perform an apparently quite different function in metabolism.

In rats deprived of vitamin B₂ (riboflavine) to just such an extent that breeding is still possible, ovulation, implantation, growth of the placenta and growth of the embryo will be normal up to the thirteenth day. If the diet is not supplemented by the thirteenth day the chondrification which begins on the 14th and 15th days and the laying down of membrane bone will be disorganized. The young rats are born with cleft palates, short mandibles and short ribs which have not fused with the sternum. The sensitive period is only a day or two and the damage is irreparable. Similar deformities do occur in man but it is doubtful whether they can be correlated with dietary deficiencies. The deformities produced by the virus of rubella suggest interference with the organizer substances. Extreme deprivation of vitamin A in farm animals will give a high incidence of foetal deformity and death.

Vitamin E deficiency in rats causes abortion and intra-uterine death and characteristic pathological changes in the uterus, but from this it does not follow that vitamin E deficiency is a common cause of abortion in the human. Results of treatment with vitamin E in the human are disappointing.

DIET REQUIREMENTS IN PREGNANCY AND LACTATION

Pregnancy.—The same principles hold good for the pregnant woman as for the non-pregnant—a good mixed diet. It should include as much fruit

NUTRITION IN PREGNANCY

By DUGALD BAIRD, M.D., F.R.C.O.G.

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THE successful outcome of a pregnancy depends upon a number of factors, such as the health and physique of the mother, the diet during pregnancy, age and parity, and the standard of medical and nursing care. When there is a high standard of living, the wastage of maternal and foetal life is low. In New Zealand about 45 out of every 1000 infants are either stillborn or die within the first month and the expectation of life is about 70 years. In Scotland, a country with much the same climate and inhabited by a people with much the same heredity, the reproductive wastage is about 65 and the expectation of life about 60 years. England and Wales occupy a position somewhere between these two.

It has been shown (Baird, 1947) that, other things being equal, the still-birth rate and neonatal mortality rate in social classes III, IV and V (the artisan and labouring classes) are two to three times as high as in social classes I and II (the professional, higher commercial and managerial sections of the community). This is due to the fact that the bigger the income the better the social circumstances and the better the health, physique and diet. It is possible that under ideal conditions the wastage of foetal life would be reduced to about 25 per 1000 births. It is difficult to say how far the expectation of life can be raised but there is little doubt that the amount of illness and disability could be greatly reduced.

THE EFFECT OF PREVIOUS HEALTH ON REPRODUCTION

It is not known how far the effect of malnutrition in the growing years will affect the ability to produce healthy children later. We know that many women in Britain are stunted because of deficient diet in youth and it is possible that other tissues of the body besides the skeleton are affected, so that even if a good diet is taken during pregnancy it may not be used to the full.

Baird (1945) has shown in Aberdeen that 26 per cent. of the expectant mothers attending the Maternity Hospital Clinic were under 5 feet 1 inch in height, and only 4 per cent. of private patients. In both groups the Cæsarean section rate in women below 5 feet 1 inch was 10 per cent., and in those over 5 feet 1 inch, 1 per cent. The average difference in height between the groups was 3 inches. Serious mechanical difficulty during labour was therefore found in the poorer sections of the community mostly among small women, suggesting malnutrition of the mother in the growing years as the cause of the difficulty.

A patient starting a pregnancy in a good state of health and nutrition may be able to withstand malnutrition during the pregnancy and produce a healthy

It is difficult to be certain of the extent to which the composition of breast milk can be altered by diet. Possibly the fat and fatty acid composition of the fat can be altered. The amount of water-soluble vitamins B and C present in the milk depends upon current intake, for they are stored in only limited amounts in the body, but vitamins A and D may be stored in considerable quantities and therefore the amounts found in milk vary less with day-to-day differences in food. Approximately 500 c.cm. of milk are required at 1 month, increasing to 1 litre at 5 months, when supplementation of the infant's diet may begin. With average efficiency of milk production the mother's requirements would be approximately 575 calories, rising to 1,150 calories, and protein 20 gm. rising to 40 gm. daily. To this must be added her maintenance requirements, 2,100 calories and 50 gm. protein. This gives daily totals of between 2,700 and 3,200 calories and 70 to 90 gm. protein or more for a moderately active lactating woman. Few women are accustomed to eat a diet that would provide 3000 calories and unless they recognize the need and know how to provide themselves with a diet of the necessary energy value without undue bulk, serious competition for supplies may result. It seems possible that this is responsible for the frequent failure of lactation in women doing industrial work and working-class women in general. The importance of a high intake of water must not be forgotten.

Supplements.—It is seldom in this country that evidence of deficiency of a single vitamin or mineral is evident, e.g. goitre requiring iodine or osteomalacia requiring vitamin D and calcium. Uncomplicated hypochromic anæmia may be cured by taking iron, but usually the diet is deficient in other respects and the best response will occur when there is an all-round improvement in the diet. In view of the difficulty in obtaining fruit and vegetables during most of the year, the orange juice and vitamins A and D capsules or cod-liver oil should be taken as issued at clinics.

WEIGHT CHANGES IN PREGNANCY

The weight gain varies within wide limits from nothing, or "a loss of weight", to over 40 lb. (18.16 kgm.). The expected gain due to the foetus, placenta, amniotic fluid, growth of the uterus, mammae, protein storage, increase in blood volume and extracellular fluid gives a total of almost 30 lb. (13.62 kgm.). The total includes an increase of 7 lb. (3.18 kgm.) of dry matter and 23 lb. (10.44 kgm.) of water of which 60 per cent. is free fluid. Since the dry matter increases may be regarded as indispensable and not likely to vary much, the great differences found in weight gain during pregnancy are possibly due to differences in the amount of water retained.

It is found that the gain in weight during pregnancy is related to the appetite but there is no obvious relationship to the quality of the diet. The weight of the baby bears no constant relationship to the weight increase during pregnancy. At the same time more information is required about

and vegetables as can be procured, a pint of milk or more daily, all the meat ration with unrationed meat and fish in addition, eggs when possible, bread and potatoes. The pre-war diet was faulty because of the unlimited quantities of sugar and "white" bread. Since bread has always been the most important constituent of the diet, especially of the poor, its quality is most important. The superior nutritive qualities of the war-time loaf are now well recognized. The present ration of 8 oz. of sugar is quite adequate for health. The figures given in table 1 are those recommended by the United States National Research Council. The value of 2,500 calories is for sedentary women and represents an increase of 20 per cent. over the non-pregnant level.

TABLE I
RECOMMENDED DIETARY ALLOWANCES
(UNITED STATES NATIONAL RESEARCH COUNCIL, 1945)

(Amount per day)										
	Cal- ories	Pro- tein gm.	Cal- cium gm.	Iron gm.	Vita- min A I.U.	Thia- min Inj.	Ribo- flavine Inj.	Nico- tinic acid Inj.	Ascor- bic acid Inj.	Vita- min D I.U.
Pregnancy (latter half)	2500	85	1.5	15	6000	1.8	2.5	18	100	400— 800
Lactation	3000	100	2.0	15	8000	2.0	3.0	20	150	600— 800

These standards have been criticized as being unnecessarily high in respect of the B vitamins and vitamin C. It is difficult to say whether or not this is so, but they are attained by that fraction of the population which shows the best reproductive performance.

McCance *et al.* (1938) showed that in poor districts where the amount of money spent on food was low, the diet of expectant mothers was deficient in protein (especially animal protein), calcium, phosphorus, iron and vitamin B₁. With increase in the income there was increased consumption of milk, fruit, vegetables and meat, and decreased consumption of bread. The women were taller and less anæmic.

Lactation.—If the food supply during lactation is restricted, there will be competition between the body and the mammary gland for the individual constituents, and the available energy must be partitioned between maintenance needs, expenditure on work, and milk production. If the intake is insufficient one or more must suffer. The capacity to produce milk is genetically determined, but in animals, at least, restricted diet prevents inherited capacity being reached. One woman may produce twice as much milk as another when both are doing similar work and eating about the same amount of the same diet. The one giving the lower yield may put on weight or may utilize food less economically.

was high (Recht, 1946). The results are conflicting, and under severe war conditions it will always be difficult to know exactly how much food the expectant mother actually does receive.

There is no justification for reducing diet during pregnancy in an attempt to produce a smaller baby, and so make labour easy. Harm may be done by undermining the mother's strength and causing some devitalization of the child.

RELATION BETWEEN FŒTAL MORTALITY AND POOR DIET

Dietary surveys.—Concrete facts about the effect of diet in pregnancy in the human are difficult to obtain. One method is the questionnaire, which has the advantage that a fairly large number of women can be handled, but even with models and pictures of amounts of the various foodstuffs it obviously cannot be a very accurate method. Daily visits to the home by a trained dietitian, involving weighing of all food used during the course of a week, is a more accurate method but is time-consuming, and requires much intelligent cooperation on the part of the patient. There is a danger also that the dietary habits may change temporarily during the course of the experiment as a result of the survey.

Feeding experiments.—A good example of this method was that carried out in Toronto by Ebbs, Tisdale and Scott (1941).

Here 380 women were studied and were divided into three groups: (a) those receiving a poor diet throughout pregnancy; (b) those having a poor diet but supplemented for the purpose of the experiment; (c) those receiving a good diet throughout. These women were simply given advice to ensure their making the best use of the money spent on food, but they were given no supplements. Group (b) was given daily 30 ounces (850 c.cm.) of milk, one egg, one orange, one capsule containing 2000 I.U. of vitamin D, and once weekly 16 ounces (454 gm.) of canned tomato and half a pound of cheese (227 gm.), also dried wheat germ. Iron was also given. It was claimed that the incidence of stillbirth and premature labour was least in group (b) and the amount of illness in the babies in the first six months of life was much less. The numbers were small, however, and the results cannot be regarded as conclusive.

WAR EXPERIENCE IN BRITAIN

One of the most striking changes in health statistics in Britain was the fall in the stillbirth rate. From 1928-38 there was no fall in the stillbirth rate, it fell from 40 to 38 in the two years before the war, and from then up to 1945 to 28. Similar changes occurred in Scotland. This fall affected all age-groups and parities except elderly multiparæ. The evidence suggests that the fall was due in large measure to improvement in the quality of the diet of expectant mothers, i.e., more milk, national bread, more vitamins and an increased awareness of the importance of good nutrition during pregnancy. There was, of course, more purchasing power. With careful shopping, energy requirements can be met, although it may be difficult to get that surplus which gives abundant energy. On the average, before the

those cases in which little or no weight increase occurs during pregnancy. This is more commonly found in elderly primiparæ and may indicate some failure of metabolism. Undue increase in weight is found in the toxæmia of pregnancy, but whether the undue gain in weight predisposes to toxæmia or whether the undue increase in weight is simply water retention resulting from the toxæmia is not quite clear.

In Germany in the 1914-18 war, the death rate from eclampsia fell markedly and this was said by some to be due to restriction of protein in the diet. The same is believed to have occurred in the recent war. Experience suggests, however, that pre-eclamptic toxæmia is considerably less common among private patients, whose diet is much more rich in protein, than among the poor. Also the death rate from eclampsia in England and Wales fell by 50 per cent. between 1939-44. One of the reasons for this is believed to be improved diet of the poorer section of the community, i.e., more milk, improved bread, the taking of vitamins and the general increased awareness of the importance of a good dietary intake during pregnancy. There is no clear evidence that it is helpful to withhold meat, eggs and milk in the treatment of pre-eclampsia. Restriction of salt and fluid intake have a beneficial effect when there is evidence of œdema.

CONTROL OF BIRTH WEIGHT

The capacity to grow and the final stature attainable are determined by genetic constitution. The capacity to grow may be modified in the first place by the size of the mother.

This was demonstrated by Hammond's (1938) experiment in the reciprocal crosses of Shire stallion with Shetland mare, and Shire mare with Shetland stallion. In each case the size of the foal was "normal" for the mother and in each case post-natal growth appeared to be a compromise between genetic urge to grow and the maternal milk supply.

It is not known whether the control of fetal growth *in utero* is due to the supply of growth hormones or of nutrients, both of which might vary with the mother's size. The physiological possibilities of controlling birth weight are restricted by the fact that within wide limits the fetus will be nourished at the expense of the mother. There is no evidence that in the human the birth weight bears any relationship to the size of the father, and predictions of difficult labour on this account have little substance. There is no close correlation between the weight gain of the mother during pregnancy and the size of the infant. Some mothers with a very good appetite during the whole of pregnancy, and who put on a lot of weight, produce quite small infants. Reports of the results of privation in Europe during the war vary in relation to the degree of privation. In Holland during the months of greatest privation many infants were underweight though not premature, but the stillbirth rate was said not to be increased and lactation remarkably little interfered with. In Budapest during a period of near starvation, birth weights were much below normal and the stillbirth rate

THE SCHOOL CHILD AND HIS DIET

By R. E. SMITH, M.B., F.R.C.P.

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IN 1945 I wrote an article in *The Practitioner* on "Diet and the School Child". Little has occurred since then to alter the basal constituents of his diet; if anything it is worse to-day if for no other reason than it is the same and therefore monotonously unvaried, and those responsible for its presentation have lost pride in its service. If we wish to improve the diet we must survey the ways and means from the very widest angles: the international, the historical, the scientific, the presentation, the production, and from the angle of those who have actually been undernourished.

THE INTERNATIONAL OUTLOOK

Professor Cruickshank in his book "Food and Nutrition" rightly draws attention to the gross malnutrition in India, China, Africa and, to a less extent, in South America. In the Orient the reliance on factory-milled rice and other cereals and the neglect of first-class protein lead to a prevalence of goitre, macrocytic anæmia, epidemic dropsy, beri-beri, and amœbic dysentery. The mortality is notoriously high and 50 per cent. occurs in children under ten years of age, five times as high as in the West. China differs little from India. In China, even in the North where the egg consumption is greatest, the average per person does not exceed one a week. Africa fares just as badly, and in the Pacific States of South America there are serious deficiencies in protein, vitamins and minerals. These countries emphasize the pathetic truth that food is poorly distributed, and we should anticipate the reaction of the natives of these countries as they become educated to the realization of this truth. They will only part with food in exchange for something they want more. The late Wendell Wilkie said in his book "One World": "It is also inescapably true that to raise the standard of living of any man anywhere in the world is to raise the standard of living by some slight degree of every man everywhere in the world". Therefore if we wish to raise our own standard of living we must start at home and hope that the repercussions will quickly raise that of others.

THE SCHOOL FARM

I have no hesitation in saying that the best fed in England are those who rely on their own energies. From mid-June to mid-September this year I visited some two dozen schools in England and America, and I came to the conclusion that the best fed schools were those which produced as much of their own food as they could.

School farms vary as much as schools themselves. At one school everything you can think of was produced on the farm. They killed one bullock, and

war one-third of the population had only from 50 to 70 per cent. of some of their requirements satisfied, one-third had just enough, and one-third had a diet with surpluses of from 10 to 30 per cent., whereas now all can just about cover their requirements. Sutherland (1946) has shown by multiple regression technique that the stillbirth rate is related, in the county boroughs, to the degree of unemployment and to the proportion of poorly paid workers, but not to overcrowding. Woolf (1947) has also demonstrated an association between the stillbirth rate and indices of economic stringency.

The importance of skilled antenatal care and obstetrical skill should not be neglected because they cannot be readily measured. The unusually low stillbirth rate in London may be due in large measure to a high standard of obstetrics. The fall in the number of stillbirths during the war years occurred mostly in the categories "prematurity" and "unexplained intra-uterine death", causes more likely to be affected by improvement in the nutrition of the mother than by improvement in obstetric skill.

SUMMARY

A good mixed diet of meat, fish, eggs, milk, vegetables, and fruit will supply all that is required for pregnancy. When the diet is deficient in quality or quantity or both, there will be a high incidence of maternal ill-health during pregnancy, including pre-eclamptic toxæmia, more premature labours, more stillbirths and more infants of poor vitality; there will be less chance of lactation being sustained. These effects will be more evident in primigravida over thirty years of age and in twin pregnancy.

It is difficult to say how much saving of foetal life would result if a first-class diet were given during pregnancy to a woman previously undernourished. The war experience suggests that the effect would be marked. Even if the food were available, a great deal of education in food habits is necessary to bring this about. There is still much to be done to see that the women in the poorer sections of the community take the priority foods and supplements available to them. Research on the physiology of human pregnancy is urgently needed since we are still ignorant of all the factors involved in the production of strong and healthy infants.

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of domestic staff. I am never tired of telling this true story:—

Applicants were being interviewed for the post of manager of an industrial canteen. One applicant surprised the selection committee by saying that if he undertook the job he made two conditions. After recovery from the initial shock, the committee agreed to hear them, which were: first, that he should not be dismissed within a month, and secondly, that he was allowed to do away with the hot plates. He was appointed and the inevitable happened. At first the customers had to wait up to five to ten minutes for their meal and they complained, but the management stood firm. Quickly they began to appreciate that the food was fresh, as it was ready to be served immediately it was cooked and they did not mind waiting for a short while. The Medical Officer to this company told me that whenever possible he visited this satellite factory at dinner time as the food was the best he could get.

Compare this with what happens in schools. I witnessed cabbage already cooked at 10.15 a.m. and being put in tureens to be kept warm in hot plates until 1 o'clock. One cook in another school proudly told me that she only kept the meat hot for 10 minutes before it was served. On being asked how she did it she said that she cooked it the day before and warmed it next day. Thousands of boys and girls must be receiving such food, the more especially as many school authorities have central kitchens from which they disperse food in heated containers.

The remedy is a return to family life or an imitation of it. How delightful it was to go to a school of 80 and see about six masters each carving for his table. No second helpings in these days cuts down the labour and service. Here is the solution. Every master should be able to carve hot and cold meat. The service of vegetables in most communities can be left to the individual, for one of the chief ideas behind the dinner at school scheme is the teaching of manners, which includes unselfishness. "Return to family-life" is important. Where is there less waste of food than in a well-run family? If it takes a generation to inculcate a new idea then let us now start on the one that the educated mother can feed her own child. The State at the present time regards the parent as inefficient. It is true the mother receives family allowances, but the mother is not trusted to give her child the extra third of a pint of milk daily nor is she allowed rations for the mid-day meal at home. If the mother is entrusted with money, surely she can be entrusted with milk and the mid-day rations.

THE SERVICE OF FOOD

I return to this important subject to relate how magnificently it is served on board ship. We have been exhorted to serve vegetables as soon as they are ready, but outside private houses I have not found anybody catering for really large numbers do this except on board ship. There the potatoes are put in boiling water, some 20 minutes, and a second lot 10 minutes, before the meal is due and this allows those who have soup to have their potatoes straight from the pot. Potatoes are such an important source of calories that it may be forgotten that they also provide vitamin C. The Irish famine of a century ago was accompanied by a definite increase of scurvy. The amount of vitamin C in potatoes is greatest in new, least in old potatoes with

one pig or two sheep once a week. Everything was used, e.g., all the offal, which has such a high nutritional value. Other schools, though they had a first-class herd of cows, did not kill to produce their own meat. Milk is still the sheet-anchor of the child's diet and those farms which have their own herds can control the hygiene of their milk supply, whereas others cannot. Another school which owns a farm was able to produce enough eggs during the war so that every boy had three a week. This has been achieved by scientific breeding. No eggs are used for hatching which do not come from pullets which had produced 200 eggs in their first year. The young cockerels were sold at an early age but were sufficiently large for the table. Let me hasten to say that all this has been achieved without any infringement of the law. That same school has made grand profits on its farm, which has produced all the fresh vegetables needed.

The farm is to the school as the garden is to the parent. The garden can augment our supplies but, what is equally important, gives us variety. The farmer is traditionally a grumbler, so often is the gardener. Last year was one of drought, and the green vegetables such as brussels sprouts and cabbage failed, but on the credit side were the wonderful tomatoes which in October were still growing and ripening, and the scarlet runner bean crop still produced tender young beans. Most individuals on their allotted rations can keep sufficient hens to produce enough eggs to emulate that school which gave their boys three every week.

THE EXAMPLE OF A PRISONER OF WAR CAMP

In "The personal experiences as a prisoner of war, with special references to Dietetics", Lieut.-Colonel J. H. Bolton, R.A.M.C. (1947), gives a good example of necessity being the mother of invention. He states that the "vegetable garden supplied limited calories but gave vitamins, minerals and variety in the form of fresh lettuce, carrots, cabbages, beans and many other vegetables". Another dictum of Bolton's is "other means of improving nutrition depend upon organization". He relates how communal cooking effected a great saving on both food and fuel and gave a greater scope for variety. This was never popular with "other ranks" who regarded a Red Cross parcel as their own property and resented "socialistic interference with private property".

THE ADVANTAGES AND DISADVANTAGES OF COMMUNAL COOKING

On my tour of schools one of my subjects of detailed inquiry at every school was the service of food. Every school was pleased to show me their arrangements. Two statements seem to be accepted. First, that feeding in large numbers is economical, and secondly, that cold meat goes much further than hot. Having seen cooking for large numbers I am convinced that the serving of an appetizing meal to any number greater than one hundred is not within the capacity of most organizers with the present-day difficulties

nourishment or malnutrition which could not be attributed to past shortages. In districts which before the war had been subject to long periods of unemployment, many of the adults and adolescents, and particularly the women, showed that they had suffered severely, but only occasionally could evidence of a present deficiency be found. Such evidence as did exist occurred in single families or persons. Very old people living alone on a diet of tea and bread often show signs of incipient scurvy, whilst a careless, thriftless or ignorant housewife with no skill or interest in cooking will undernourish her family whatever her husband's earnings may be" ("On the State of the Public Health during Six Years of War," 1946, H.M.S.O. p.119).

Professor Sydenstricker's time was not wasted because he showed many doctors and medical students here the deficiencies which he was accustomed to see in the "poor whites" of Georgia, and gave the average student an idea of vitamin B deficiencies so that he would be able to recognize such deficiencies in the rare cases occurring in England. In the same Report it is related how vitamin supplements administered to several thousand children, and compared with a control series, had no demonstrable effect. All this went to prove that our diet, although monotonous, was not lacking in essentials. Another study along similar lines has been carried out by Miss Widdowson (1947), and hers is different in that she has studied the individual child as opposed to the mass. Perhaps her most important conclusion is summarized thus:—

"The one outstanding fact, which has been brought out again and again by this investigation, is that similar individuals may differ enormously and unpredictably in their food habits. This applies with great force to the energy value of the diets, but it is equally true of the proximate principles, minerals and vitamins, and still more true of the foods themselves. These extraordinary departures from the average are compatible with normal physical development. These findings indicate that individual requirements must differ as much as individual intakes, and that an average intake, however valuable statistically, should never be used to assess an individual's requirement".

Other historical facts are that educational authorities have refused to allow children to help with agriculture in school hours, and that some schools have discontinued to organize holiday camps since the war because they thought the danger was over.

SUMMARY

If nutrition is to be improved, the following principles should be adopted:—

(1) Family life, or a recognizable imitation of it in schools, should be encouraged.

(2) This applies in particular to service and the provision of variety.

(3) Cooking should be regarded as an art and not as the mere chemico-physical preliminary to mastication.

(4) Education in food values is desirable and the criterion of a good food should be judged by whether or not it is able to support life. By this token, milk, eggs and wholemeal bread are foods of high biological value.

(5) The preservation and hygiene of food stocks are important.

(6) Last, but most important, is that the need for helping ourselves and not relying on others, even if we are being educated or are educators, is as important to-day as in war time.

a gradual diminution as time advances, but that is no reason why the little they contain should be destroyed by improper cooking. Old potatoes as well as new potatoes should be cooked in boiling water and not put in cold and brought to the boil.

The service really depends upon individual efforts of the community. The idea that cold meat goes further than hot is purely imaginary from a nutritional viewpoint. That hot meat is more difficult to carve is admitted, but practice makes perfect.

THE TIME OF MEALS

It is only just over thirty years ago that any school had a "substantial dish" for high tea: before that all that was provided was a very plain tea and some schools have only provided supper within the last ten years. Anyone wishing to gather any idea of the advance in diet in residential schools has only to read the historical introduction to the Medical Research Council's report "Epidemics in Schools" or Dr. Friend's book "The Schoolboy and His Nutrition", or the layman may know about it from Charles Lamb's essays. The ideal arrangement of time of meals must include adequate spacing. Breakfast at 8, dinner at 1 p.m. and supper at 7 p.m. are good times if these meals are adequate. In America I was struck by the saving of time and the healthiness of the American child who was fed at these times and had nothing in between, except possibly a glass of milk at night.

Habit is a great force: witness our sugar habit now deep-rooted after a century. Afternoon tea is an ideal waste of time, except as a medium for exchange of views. Is it fair to expect a boy who has violent exercise in the afternoon to go without food from 1 p.m. to 7 p.m.? Certainly, but only if that meal which is being served at 7 p.m. is a very substantial one, as indeed it should be. All schools can avail themselves of the extra rations allowed for the midday dinner, so that they have all the meat ration and points for breakfast and the evening meal, which we may call supper. It seems reasonable to make this the main meal of the day. Domestic problems must be solved, if need be by service by the boys. The ideal service by boys is that organized by Kent School, Connecticut (the winners of last year's Ladies' Plate at Henley), where every boy, irrespective of age or station, has to do his work for the "domus".

SOME LESSONS FROM RECENT HISTORY

In 1942 one of those paradoxes which surprise medical scientists occurred. Professor Sydenstricker, from Georgia, came to London on the instructions of the Rockefeller Institute to investigate deficiency diseases among children. He was aided by Dr. Stannus and Dr. Hawes, both of whom had long experience of deficiencies in the Colonies.

"Their findings were unexpectedly satisfactory, for even although they paid most attention to poor areas they found surprisingly little evidence of under-

differs little from that in Britain, but in each individual State a further examination is necessary for licence to practice and as a rule a period of internship is required before this examination can be taken. Specialists in America are recognized by their Board certificates; one central Board controls specialization throughout the country and maintains a register of fifteen different specialties. There are varying requirements before examination in each of these but several years' postgraduate work under recognized teachers is always necessary. In the case of general surgery and general (internal) medicine five years must elapse following qualification, three of these being spent in an approved hospital residency.

STREPTOMYCIN IN TUBERCULOSIS

The exact place of streptomycin in the treatment of tuberculosis is not yet decided, but more and more encouraging evidence, clinical, radiological and histological, is accumulating as to its usefulness, and certainly it has changed the hitherto hopeless outlook in acute miliary disease. The first investigation was undertaken in 1944 by Hinshaw and his colleagues at the Mayo Clinic, and subsequently other groups have carried out trial studies. The largest series of patients analysed so far has been over 800 treated by the Veterans Administration, the Army and the Navy, whose work has been carefully coordinated to ensure so far as possible uniformity in case selection and treatment. In this large group of patients there were 24 with proved *miliary tuberculosis* of the acute disseminated type treated in V.A. hospitals before May, 1947, and so far there have been only 5 deaths. In miliary cases the clinical response to streptomycin is often immediate and dramatic and healing can be shown radiographically (see fig. 1). The complication to be feared most is the development of *meningitis* during treatment: 31 of 78 cases of tuberculous meningitis treated at the same hospitals are still alive, but only 9 are free from evidence of active infection, and the known tendency of such cases to relapse makes the prognosis doubtful even in these. However, tuberculous meningitis may not always be fatal, for at the Mayo Clinic there are several patients alive some months after the end of prolonged treatment and one shows no residual signs.

More time must elapse before the permanence of the results in *pulmonary tuberculosis* can be assessed. It seems probable that in this disease the final place of streptomycin will be as an adjunct to other measures, being reserved for recent acute and progressive cases and for use in tuberculous patients undergoing surgical procedures in order to prevent spread of infection. Patients responding or likely to respond to the conventional forms of treatment should not be given streptomycin. Chronic non-progressive fibrocavous and cavernous types and terminal cases with bilateral destructive disease are not suitable subjects; for streptomycin will only be of benefit if natural healing can gain ground in the few months during which the tubercle bacilli remain sensitive to the drug.

The results in *laryngeal and tracheo-bronchial ulceration* have been

SOME PRESENT TRENDS IN AMERICAN MEDICINE

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THE recent war has brought about changes in the background of American medicine which are showing their effect in the speed of medical advances. When one considers how much was achieved by large-scale research under war-time conditions it is obvious that if such combined efforts were continued in peace the resulting benefits to humanity would be very great. Following the war, one of the most important features has been the continued cooperation of all branches of the medical profession in this country. Team work, which is so essential in the smallest medical group, is flourishing at the highest level and as a result the next few years will undoubtedly bring advances in knowledge which before the war could not have taken place in so short a time. The National Research Council is largely instrumental in bringing together the best brains in research, and an almost unlimited field is at their disposal. The N.R.C. has funds for research projects approved by its committees on all medical and surgical subjects, and these committees consist of representatives from the civilian profession and all the services. In America, every ex-serviceman is entitled for the rest of his life to treatment from the Veterans Administration, and the fact that the war-time Army alone was over eight million strong indicates the scope for research workers and statisticians in the follow-up investigation of medical and surgical conditions. As well as the medical conditions which are more peculiar to war there are large series of all groups of diseases, the continued study of which will be of value; for example, coronary disease, the incidence of which was unexpectedly high amongst young men in the Forces during the war. There is still wide scope in the Army and the Navy for research in clinical and preventive medicine: for instance, the Army has established research centres for the study of infective hepatitis in all areas where large numbers of troops are serving and the Navy has a big hospital in the State of Georgia given over entirely to the investigation of rheumatic fever.

Apart from these large-scale projects, smaller research groups are active at all medical centres in America. Some are privately endowed, some are financed by the large pharmaceutical firms, whose own research laboratories are among the finest, and others are sponsored by the life insurance companies. The spirit of research, for which American medicine is justly famous, is imbued in the student early in his career. In most States there are fewer restrictions governing animal experiments than in Britain, and such work is a most popular feature amongst students. It also forms a most important part of postgraduate training. The average age of graduation



FIG. 1.—Miliary tuberculosis before and (right) after three months' treatment. This patient relapsed later and died of tuberculous meningitis (By kind permission of the Tuberculosis Division, U.S. Veterans Administration)



FIG. 2.—Extensive tuberculous ulceration of the tongue before and (right) after three months' treatment (By kind permission of the Tuberculosis Division, U.S. Veterans Administration)

STREPTOMYCIN IN TUBERCULOSIS

dramatic, all lesions healing rapidly within ninety days of the start of treatment (fig. 2). By inhalation alone the drug has proved unsatisfactory in these cases and combined intramuscular and aerosol administration appears to be the best. In *tuberculous sinuses* and *lymphadenitis* streptomycin has proved very successful and its effects in some cases of *pericarditis* and *lupus vulgaris* (fig. 3) have been encouraging. *Tuberculosis of the alimentary tract* has responded clinically in a dramatic way, with relief of diarrhoea and gain in weight, and some cases of *peritonitis* have cleared up rapidly. No conclusions can yet be drawn as to the usefulness of the drug in bone and joint tuberculosis or in renal disease, but some cases of the latter have improved and become symptom-free although still passing occasional tubercle bacilli in the urine.

Streptomycin resistance.—The tubercle bacillus is very sensitive to streptomycin *in vitro*. During treatment it remains so for several months before becoming resistant and this period often allows good results to be obtained. Resistant tubercle bacilli probably appear in at least two-thirds of patients after less than 120 days of treatment, but a great deal more evidence will be necessary before the situation can be stated definitely.

Dosage.—The optimum dosage and duration of treatment have yet to be determined. The dosage usually employed now is 2 gm. daily—0.4 gm. intramuscularly at four-hour intervals from 8 a.m. to midnight—for 120 days. Streptomycin is not absorbed into the blood stream when given by inhalation or orally. It is very effective by the latter route in the preparation of patients for colonic surgery, as it practically sterilizes the bowel.

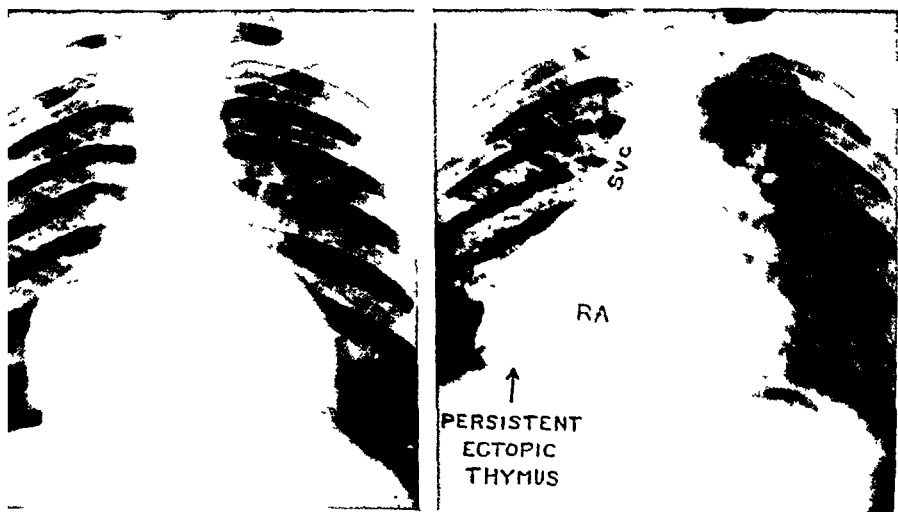
Toxicity.—Most patients receiving the above dosage have developed signs of eighth nerve damage. Vertigo of varying degree usually appears in the fourth week, but this lessens and often disappears during continued treatment although the caloric tests remain abnormal for many months and in some cases possibly permanently. The auditory branch of the eighth nerve is affected only rarely. Local irritation, originally frequent, is now less common with the purer preparations in use. Fever, blood dyscrasias and sensitivity reactions also may occur; the last of these responds to the anti-histamine drugs. Generalized exfoliative dermatitis has been ascribed to streptomycin. Periodic albuminuria with casts is common and when there is pre-existing renal dysfunction, evidence of renal inefficiency may appear, in which event the treatment should be stopped. Although streptomycin may occasionally produce severe toxic effects during the long treatment of tuberculosis it appears to be entirely safe when used in short courses for acute infections such as tularæmia and meningitis due to Pfeiffer's bacillus, in both of which it has proved life-saving.

THE TREATMENT OF CONGENITAL PULMONARY STENOSIS

Until Gross in Boston successfully closed a patent ductus arteriosus in 1938 there was no curative treatment for congenital heart disease. This marked a new epoch in cardiology and there followed in 1944 the cure of coarctation



5.—This tumour, shown by cardio-angiography (right) not to be an aneurysm, was found at operation to be a branchogenic cyst, which was successfully removed. (Fig. 5-9 are reproduced with permission of Dr. George P. Robb.)



6.—Here apparent enlargement of the heart shadow is proved (right) to be caused by an extra-cardiac mass

CARDIO-ANGIOGRAPHY



FIG. 3.—*Streptomycin in tuberculosis.* Lupus vulgaris before and (right) after treatment—115 days after streptomycin in 117 days. Great improvement was seen but biopsy after the course of treatment showed that typical tubercle formation was still present. (By kind permission of Dr. Paul O'Leary and the *Archives of Dermatology and Syphilology*.)



FIG. 4.—*Surgical treatment of congenital pulmonary stenosis.* Photographs taken before and (right) two weeks after operation. The originals were in colour but improvement is obvious even in black-and-white reproductions. (By kind permission of Dr. Alfred Blalock.)

of the aorta by Crafoord in Sweden. In the same year, Blalock in Baltimore carried out his first operation on a child with congenital pulmonary stenosis (fig. 4). No apology is needed for including this surgical triumph in an article on medical trends, for it was the result of a physiological approach to the problem of improving the function of an essential structure, and there can be no better example of what American research methods can achieve in the clinical field by team work.

The most common congenital cardiovascular defect with cyanosis is the *tetralogy of Fallot*, in which there coexist pulmonary stenosis or atresia, interventricular septal defect, dextraposition of the aorta and right ventricular hypertrophy. The cyanosis is due to three factors: shunting of venous blood into the systemic circulation, poor oxygenation of the blood in the lungs due to pulmonary changes, and reduced volume of blood reaching the lungs for aeration. The importance of the last factor was first realized by Dr. Helen Taussig, and Blalock's work was stimulated by her belief that patients with pulmonary stenosis would be benefited if a means of increasing the blood supply to the lungs could be devised. This has been done by making an artificial ductus arteriosus. Before undertaking operations on humans, many experiments were done on dogs, and eventually bilateral pulmonary arteriovenous fistulæ were produced with resulting reduction in the oxygen saturation of the arterial blood; this was increased when an artificial ductus arteriosus was made. Any scepticism regarding the benefits from establishing an artificial ductus in cases of Fallot's tetralogy has been dismissed by the brilliant results. The ductus is made by anastomosing the proximal end of the divided innominate or left subclavian artery to the side of the right or left pulmonary artery, according to the side on which the aorta descends, which is a variable factor. Most children have survived the operation, and the collateral circulation to the arm is adequate. Several days after operation, decrease in the cyanosis of the lips and finger nails is apparent as the oxygenation of the blood improves and the polycythæmia diminishes, and subsequently exercise tolerance increases, clubbing of the fingers lessens, and previously stunted children begin to develop.

Careful diagnosis and selection of cases for this operation are essential. Apart from routine clinical, radiographic and electrocardiographic examinations the systemic and pulmonary blood flow and arterial saturation with oxygen are determined, venous catheterization being employed, and the chambers of the heart and the great vessels are visualized by cardio-angiography. These newer investigations are important as they help to eliminate cases of cyanotic congenital heart disease, such as the Eisenmenger type, in which the operation is not indicated. On my last visit to Blalock and his associates they were operating on their four hundred and fifty-ninth case. So far, the over-all mortality has been 18 per cent., including deaths amongst those in whom an anastomosis could not be performed, those in whom the diagnosis was in error and those who have died since leaving

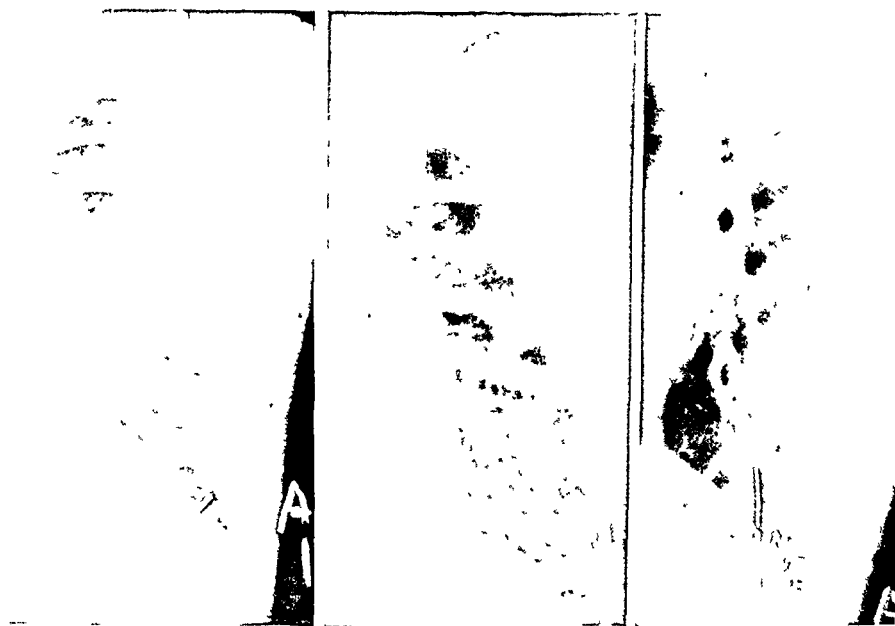


FIG. 7.—The diagnosis of pulmonary arterio-venous aneurysm.



FIG. 8.—The diagnosis of fusiform aneurysm of the aorta.



FIG. 9.—Coarctation of the aorta.

or treatment. Continued research into its etiology is being carried on by many groups. The surgical treatment of hypertension, which has been in use in America for over twenty years, now usually comprises an extensive bilateral thoraco-lumbar sympathectomy. This produces widespread vasodilatation, and its purpose is to lower the blood pressure by reducing peripheral resistance in addition to denervating the kidneys and suprarenals, which can be explored for possible tumour at the operation. It is often strikingly effective in carefully selected cases, relieving headache and giddiness; comparatively young patients who have been incapacitated by severe symptoms have been rendered fit to go back to work. Thus the operation is frequently of great value both clinically and economically. Such results provide an answer to arguments against surgery on the grounds that it is unjustified, being symptomatic and not curative treatment. Since in hypertension the expectation of life is not easy to predict it is also difficult to decide whether it is prolonged by sympathectomy. However, in many cases it has made life more bearable.

In medical treatment there are under investigation drugs which block adrenergic effects, and drugs inhibiting the ganglionic transmission of nerve impulses in the autonomic system, such as tetra-ethyl ammonium bromide. Psychotherapy has gained ground in the treatment of the anxiety which is so often a feature in hypertension. The importance of *dietary sodium chloride and water intake* is receiving attention, particularly in the late effects of hypertension. Recent work by Gorham in Albany has shown that in congestive heart failure a diet containing 1 gm. of sodium chloride and 3000 c.cm. of water daily is far superior to the conventional 3 gm. of salt and 1,500 c.cm. of water, and that forcing the intake of fluids above 3000 c.cm., which has been advocated by other workers, is of but little added advantage. In the majority of 22 patients the œdema subsided within one week; only 5 responded poorly and these were chronic cases with long-standing œdema. None of the patients under treatment was receiving mercurial diuretics.

PROPYL THIOURACIL IN THYROTOXICOSIS

On account of the toxicity of thiouracil, propyl thiouracil is rapidly replacing it in the treatment of thyrotoxicosis in America. A dosage higher than that originally used is now found necessary—Lahey in Boston advocates 200 to 225 mgm. daily. Iodine is given concurrently in the preparation of the patient for surgery, as otherwise the thyroid remains hyperplastic and thyroidectomy is difficult. Thyroid extract has also been found to produce involution in the gland when given instead of iodine with thiouracil. The persistence of hyperplasia during treatment with propyl thiouracil is cited as evidence that the drug is not a substitute for surgery, but its use has made the preoperative phase of thyrotoxic cases very smooth, and pregnant patients, psychotics and diabetics have all responded well. On propyl thiouracil the basal metabolic rate has been found to fall at the rate of about

hospital. Only one case has developed infection with *Streptococcus viridans*, and this has been cured with penicillin.

VISUAL METHODS IN TEACHING

Colour photography has been developed to a fine art and allows graphic records to be kept of cases, fresh pathological specimens, operations, and even fundi. Sound films covering the basic sciences and all branches of medicine and surgery are used in teaching at all medical schools, and the Surgeon General has arranged for a comprehensive selection to be available on loan in Britain. For some time the possibilities of *television* have been considered and these were realized when the Blalock operation was successfully relayed last year to a large medical group which was meeting at the Johns Hopkins Hospital.

CARDIO-ANGIOGRAPHY

The use of this procedure in the diagnosis of congenital heart disease has already been mentioned. It has also proved helpful in localizing foreign bodies in the heart and in the diagnosis of pericardial effusion. It is being used more and more widely in America in the elucidation of mediastinal shadows seen in straight skiagrams of the chest, and decides definitely whether or no they are caused by cardiovascular abnormalities (fig. 5-9). In these days of sweeping advances in thoracic surgery cardio-angiography is being recognized as an essential investigation in most cases of obscure intrathoracic conditions. It is the only means, for instance, by which pulmonary arteriovenous aneurysms can be diagnosed accurately. These are being found not uncommonly in cases of hæmoptysis of uncertain origin. The procedure at first may seem complicated and it is uncomfortable for the patient, but it often saves much time which would otherwise be spent in prolonged investigations. Also, it has spared patients from surgical exploration of the chest and from empirical radiotherapy for undiagnosed mediastinal tumours.

The method, originally devised by Robb and Steinberg in 1938, consists of the rapid intravenous injection of 50 c.cm. of 70 per cent. "diodrast" (in Britain, "perabrodil") into the principal antecubital vein. This passes on to the heart, pulmonary and systemic vessels as a bolus during the first circulation, and skiagrams of these structures must be taken at the exact time when they are opaque. The times for exposure are calculated beforehand after determining the "decholin" arm-to-tongue and the ether arm-to-lung circulation times. There is a reaction lasting some minutes following the injection of diodrast; a metallic taste and a wave of intense burning starting in the mouth and spreading through the whole body.

No fatalities have occurred as the result of cardio-angiography and it will undoubtedly add to our knowledge of mediastinal, heart and lung disease, and simplify the teaching of anatomy and physiology.

HYPERTENSION

This condition is kept in the lay mind by insurance advertisements and by the popular press, which is always ready to publicize any new line of research

THE DEPRESSIVE PERSONALITY IN GENERAL PRACTICE

By WILFRED LESTER, M.B., B.S.

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No psychiatric condition is more protean in its manifestations than depression. From the mild fit of the blues following influenza to the abysmal depression of the suicidal melancholic it pervades the whole range of psychiatry in both its organic and functional (psychogenic) aspects. Nevertheless, a characteristic common to most depressive states, no matter what their precipitating cause, is the factor of constitutional tendency or predisposition as embodied in the basic personality. This is best illustrated in such affective psychoses as endogenous or constitutional depression occurring at any age, involutional depression of the climacteric, and the senile depression of the aged. In such cases there is usually a significant family history, often including suicide, and a significant personal history, which, if taken painstakingly enough, usually reveals the roots of the depressive personality.

THE IMPORTANCE OF THE BASIC PERSONALITY

Although the family doctor is seldom called upon to treat the major psychotic depressions, some knowledge of the basic depressive personality will be of inestimable value to him in treating the hundreds of minor depressions he sees following such common infective illnesses as influenza, pneumonia, hepatitis, and the like. Thus, in the case of post-influenzal depression the most important factor in prognosis is the basic personality of the patient. For example, if he were previously active, cheerful and sociable, without obvious faults in character or temperament, that is to say, if he were a well-adjusted personality, the prognosis would be excellent. He could be told with confidence that he would be fit within a week or so. If, on the other hand, the basic personality is poor, the prognosis is correspondingly poor. Thus a post-influenzal depression occurring in a timorous, diffident, over-cautious, over-sensitive individual, not much given to social activity, is likely to be prolonged. This inhibited personality, never enamoured of the outside world, reacts negatively to the stress and strain of everyday life. He is always ready to give up things. If he catches cold frequently (itself a neurotic phenomenon more often than not) he will give up either games or smoking or drinking or tea or sex, all if necessary, in the hope that such self-abnegation will protect him from future evil and thus ensure that absence of illness which to the depressive personality constitutes good health. If the world is too difficult he will renounce it and

one point daily in primary thyrotoxicosis; in cases of toxic adenoma the response is much slower. Propyl thiouracil is a safer drug than thiouracil but some 2 per cent. of cases have developed agranulocytosis. Since this may appear up to seven days after the drug is stopped, for reasons of safety none is given for ten days before operation. Thiouracil has been used successfully in cases which have developed agranulocytosis following propyl thiouracil, and it is generally agreed that these few are the only cases for which thiouracil should now be used. When agranulocytosis occurs the patient is protected against infection by the use of penicillin. The early mild thyrotoxic patient for whom conservative treatment might have been tried previously has been found by Rose of Philadelphia to have a 50 per cent. chance of permanent remission after twelve months' treatment with propyl thiouracil alone.

THE CANCER CAMPAIGN

Almost unlimited funds are available in America for this, and a nationwide drive is in progress. Much original research work has already been carried out into the nature of malignant tumours. To give one instance: at Yale the pathology of cancer is being taught as a living subject and a museum which previously contained preserved specimens now houses several thousand animal cages. It has been found that only embryonic and malignant tissues can be transplanted into animals of different species, and this important finding is being used in the diagnosis of malignancy and in the study of carcinogenic and therapeutic substances and the evolution of transplanted tissues. The Rous sarcoma, for example, was transplanted into the anterior chamber of the guinea-pig eye and this produced an alteration in the properties of the virus.

Recent advances in nuclear physics are providing research workers with increasing numbers of radio-active substances for investigation. Great attention is being paid to the education of the public and of the medical profession in cancer problems. All medical centres are establishing regular postgraduate courses in diagnosis and treatment for general practitioners. An impressive feature in the clinical programme of many large hospitals is the "tumour board", which, like the clinico-pathological conference, is attended by representatives of all departments, residents, interns and students. Every case in which neoplasm is suspected or diagnosed is considered by this board and after free discussion the best line of treatment is decided. This is obviously of great advantage to the patient, ensuring the best chance of cure, and the educational value of such conferences both for the students and the staff needs no emphasis.

My grateful acknowledgments are due to the Surgeon General of the U.S. Army and to the Director General of our Army Medical Services. The appointment which I hold in America results from their determination to maintain the close liaison which flourished between their two Services during the war. I have also to thank all the American colleagues who have been so generous in freely discussing their work with me, and Colonel F. S. Gillespie, my predecessor, for his kind help.

workaday environment. Thus, faced with a case of acute endogenous depression, the family practitioner, armed with a knowledge of the previous personality, culled from many years of close and frequent contact, is in a position to trace the actual attack to its earliest manifestations in childhood and infancy, and thus render valuable aid to the psychiatrist, with whom he should cooperate to the maximum advantage of the patient, his family and himself.

PSYCHOPATHOLOGY OF THE DEPRESSIVE PERSONALITY

The adult.—The outstanding feature of the depressive personality is the negative or inhibited attitude towards life. He (or she) is quiet, unassuming, diffident, moderate in habits and lagging in company. He is usually precise or niggardly in speech, careful with his money, and excessively conventional in dress. In short, he makes no effort to shine. Not that he shuns worldly success: on the contrary he often achieves this, but in a slow but sure, solid, unostentatious manner. Being sound rather than brilliant, there is no flamboyance, no blowing of trumpets. His essential reserve is quite unaffected by worldly success—he does not give himself readily to anything or anybody—in effect, he neither shows nor gives feeling. Feeling is reserved for himself. He is the arch-self-lover, the arch-narcissist. If he acquires beloved objects, e.g., a wife or property, these are incorporated as part of his personality and serve to minister to his self-love, his self-esteem. If, on the other hand, beloved objects are lost (if for instance his wife dies) the grief of the depressive personality may be boundless in its intensity. Like Rachel, he may refuse to be comforted. Such a case may well end in an acute depression which would signify the collapse of the personality in the face of an unbearable loss of external supplies to his self-esteem. The inconsolable patient, in his interminable flow of self-reproaches and self-denunciations, is in reality execrating and accusing his departed beloved. In effect, there is unleashed a veritable deluge of unconscious sadistic hate directed against the departed loved one who dared make such a breach in his exaggerated and tender self-esteem. These sadistic attacks are accompanied, however, by a heavy load of guilt feelings which manifest themselves in such negative behaviour (self-punishments) as not washing, not eating, not sleeping, not wanting to live, and so on. Thus is the sadistic hate neutralized or expiated.

The child.—The depressive child personality usually expresses itself in behaviour peculiarities. Again, inhibition and negativism are the conspicuous features, no matter how masked they may be by superimposed activities. For instance, a child who is fond of solitary walks may be actuated by the desire to get away from her playmates, and not to explore new places and new people. This is negative activity. Children who are “as good as gold” never ill-mannered, never unkind or aggressive, who never “give a day’s trouble” are inhibited children. These are the children who, although they never rough and tumble with their playmates, are always falling and hurting themselves. They are not keen on going to the pictures or parties

seek fulfilment in himself. If the world does not love him he will love himself. Hence the psycho-analytical designation of the depressive as the narcissist and the depression state as a narcissistic neurosis.

Apart from the constitutional factor the measure of a depressive's love of self is a measure of the rebuffs he has suffered from the outside world, e.g. loss of a beloved relative, loss of health, loss of money. Thus a post-influenzal depression occurring in an inhibited personality may well end in a hypochondriacal depressive state in which the irrational and morbid preoccupation with his bodily condition is but a measure of the amount of libido (instinctual energy) withdrawn from his immediate environment (e.g. wife, work, social interest) and lavished on (introjected or incorporated within) himself.

The family practitioner sees hundreds of cases of simple toxic depressive states and he can do valuable prophylactic work in the recognition and evaluation of their personality factors and in the re-education, reassurance and insight he can offer in consequence. Usually the practitioner attributes a prolonged convalescence from a bout of influenza, for example, to the severity of the attack. This is not so. In the depression following such severe attacks, the good personality convalesces quicker than the poor personality. When the influenzal attack itself is over within forty-eight hours, as it should be in an uncomplicated case, the prognosis of any post-influenzal depression rests on psychogenic and not somatic factors. I have stressed this point because medicine even to-day is still imbued with an unduly materialistic outlook. We are still inclined to think in terms of the sequelæ of a disease rather than of the after-effects of a disease on a dynamic personality. The same considerations apply to some extent to such organic depressive states occurring in cerebral arteriosclerosis, cerebral syphilis, and even in general paralysis in which depression occurs instead of euphoria.

It is, however, when we come to consider such psychogenic depressions as endogenous or constitutional depression and involuntional melancholia that the factors of basic personality and narcissistic withdrawal of affect (feeling) emerge as powerful pointers in the further understanding of the psychopathology and in the evaluation of the course and prognosis of the disease. It has already been stated that the hereditary factor is prominent in the etiology. This is obvious, and needs no further comment. What is equally important (particularly in prognosis) but not so obvious is evidence of the pre-existing depressive personality. The supreme importance of the recognition and assessment of pre-existing depressive factors in the personality cannot be exaggerated, for, no matter what therapy be applied, and no matter how successfully, in combating an actual depressive attack, the ultimate prognosis depends almost exclusively upon the relative strength or weakness of the personality previous to the attack.

In the appraisalment of the previous depressive personality, none is better placed than the family practitioner, for he has probably known the patient and his family for many years, and is familiar with his social and

in spite of her husband's gloomy forebodings, began to wax cheerful and optimistic and looked forward with eager anticipation to the birth of her son who one day would shower on her all the good things her husband was incapable of providing. Such were the circumstances attending the birth of her second child, another daughter. Her disappointment was inexpressible, and although she was a dutiful and hardworking mother she found it impossible to suppress the bitterness and rancour that oppressed her heart. She accepted her baby physically (that is to say, she fed it, clothed it and sheltered it adequately) but rejected it emotionally. The baby is not born who does not feel when love is being denied it, and so it proved with our patient. When her brother was born fifteen months later, her rejection was complete. At sixteen months, before she could walk or talk, her large sad, all-comprehending eyes would watch her mother fondle and hug her baby brother and she would wonder in her poor starved little soul what terrible crime she must have committed that she should be denied such ecstasy.

Thus she grew up, inwardly craving for the love always denied her and inwardly accepting her own wicked thoughts of revenge and jealousy as sufficient to disqualify her from participating in any such felicity. Her mother said she was always a good child, reserved and sensitive perhaps, but ever thoughtful for others and never disobedient. But this was not so. She was unloved, and she hated, with a hate that was terrifying, the mother who had rejected her. In reality she was a child who carried a merciless load of unconscious guilt that marked her off from her playmates. If other children were bright, noisy and cheerful, they had every right to be so. They had committed no crime (the crime of hating mother) that lay on their conscience and so made them unloved. If she was timid and obedient, how else could she show her penitence?

Thus she grew up into womanhood. Never having received love, she was incapable of giving it. On the other hand, her craving for love was insatiable. Criticism for her was intolerable, for that meant further loss of love. Thus when the forelady at work spoke to her a little sharply, she remained silent, but was taken ill the same night, developed influenza the next morning and kept to her bed for a week. A fortnight later occurred the fatal quarrel with her young man. He was her first love, and like the starved animal she was, she fed greedily and with an appetite for his attention that was insatiable. She was ever eager to receive, although quite incapable of returning his tender advances. If he did not smile when she thought he should, she would sulk for the rest of the evening. If he were so much as a minute late, or his tie were not to her liking, he never heard the end of it. He was her first "love-object", and she intended to possess him lock, stock and barrel. The past would be well and truly compensated for. Alas for all her high hopes! Her fiancé, full of manly ardour, sought vainly for a similar feeling in his beloved, and this disappointment, added to perpetual bickering over petty differences which came to a head during her convalescence, decided him to break the whole thing off. For the poor girl (now a woman of thirty) this was catastrophe, complete and shattering. Her sense of guilt, lately subdued in her newly-found love, again reared its ugly head and nothing now could persuade her that she was not an unworthy guilt-ridden creature who must expiate the wickedness within her. Life was not for her. Why work, why eat, why live?

In this simple case of depression (precipitated as it may have been by influenza, an unhappy love affair and difficulties at work), the roots of the depressive personality are clearly visible through the morass of superimposed environmental stress. And so it is with hosts of similar cases, many of which could be ameliorated, if not prevented, by an earlier and more comprehensive appraisal of the situation by the family practitioner, who, in his general approach, should be influenced less by material causation and more by psychogenic motivation. Thus he would see his patient less as a case and more as a dynamic personality.

(except their own), and can always be left alone with the confident knowledge that they will not get into mischief. At school they may be good or average at games or lessons; they never enthuse. They are not inquisitive. They are seldom interested in the "facts of life" and usually acquire them much later than the average child. They are poor or finicky eaters, in spite of which their physical development continues unimpaired. Too often they are harassed mothers' favourites: "she is so good I do not know she is there" or "she is as quiet as a mouse, bless her". Thus the depressive child reaches adolescence often extolled, never suspected.

The depressive infant.—Some psychoanalysts go so far as to assert that all infants pass through a depressive phase on account of the guilt feelings evoked by the fantasied all-devouring attacks on the frustrating breast. Be that as it may, to the practitioner the depressive infant is the one who, finding his excessive oral needs (constitutional tendency) frustrated, shows his displeasure initially by loud and insistent screaming, and later by a strategic passivity as if concluding that discretion, after all, is the better part of valour. When his initial attacks of rage have subsided, the infant, his baffled fury repressed, withdraws interest from his immediate environment and lapses into apparent quiet content. Thereafter (from six to twelve months) he is the good baby, so good in fact that the proud mother will often remark "we don't know we have a baby". Nevertheless, this baby develops slowly (inhibitedly): he stands, talks, toddles and explores later than the average infant, and is never happier than when he can hang on to his mother's apron strings. Thus the negative and inhibited characteristics of the depressive personality can be traced throughout life from infancy to senility.

AN ILLUSTRATIVE CASE

A brief case history illustrates certain aspects of the depressive personality:—

The patient is a young woman aged thirty, the daughter of an insurance clerk. She has been attending her panel doctor for about a month complaining of tiredness, loss of appetite, loss of weight, and loss of interest in life generally. She was sent to hospital where physical investigation proved negative, and was referred back to her doctor as a functional debility following an attack of influenza which occurred a week or two before the onset of her symptoms.

The history is as follows: She was the second of three children. Her elder sister was healthy and happily married. Her brother, fifteen months younger, was unmarried, happy-go-lucky, and quite fit. It soon became clear that this brother was the mother's favourite child. He was "her boy". The mother was an ambitious and forceful personality whose secret aspirations in life had been frustrated by a husband who put security before all else. He had also suffered a nervous breakdown early in his married life when he was incapacitated for nearly twelve months. Disappointed in her own life, the mother was determined that her son should make good all that a weak and unambitious husband had denied her. If her first child was not the boy she longed for, at least it was her firstborn, and providence would be kinder next time. But "next time" was to be five years later, and during that period affairs had not prospered for the family. Her husband had suffered a further bout of his "nervous trouble" and he was now earning less than formerly. It was at this juncture that the mother, more embittered than ever, became pregnant again and,

CLINICAL FEATURES

Admitting that pandemic and interpandemic influenza are almost certainly caused by different viruses, the authors still urge, and rightly, that really careful study of the latter, especially in its local form, may well give rise to clues as to how this type of virus infection may be influenced prophylactically and therapeutically. Their review of the Groningen outbreak of 1941 is designed to that end and makes some useful points. The incubation period was noticeably short and corresponded to the well-known case of Stuart-Harris who developed the disease forty-five hours after being infected by a sneezing ferret. The sharp rise of temperature, headache, body pains, particularly in muscles and joints, pain on moving the eyes and insomnia and restlessness all showed their usual high incidence. A characteristic phenomenon was the pharyngeal reddish-blue hyperæmia with scattered white, pin-head vesicles. Acute tonsillitis was rarely observed. The blood changes in uncomplicated cases were leucopenic with a striking virtual disappearance of the eosinophils.

The sputum was slimy and full of desquamated epithelium from the bronchi. It rarely became purulent, corresponding to the fact that in infections of experimental animals there is very little purulent pulmonary exudate. Pus in quantity evidently implied secondary bacterial invasion. Particular attention was paid to both the bacteriology and the histology of the sputum, and the findings support the view that, in this interpandemic disease at least, the virus itself causes a peculiar degenerative-regenerative lesion in the mucous membranes of the nose, trachea, bronchi, bronchioli, and probably also of the alveolar epithelium of the lung. Thereafter the nature of any secondary bacterial invasion must decide the course of the illness. In the initial virus infection the essential lesion of the mucosæ is characteristic and may be diagnostic for autopsy purposes. Infectivity of sputum was recorded as lasting up to one week or more.

CONCLUSIONS

Most of the results confirmed that the outbreak was caused by virus A and that many of the recovered patients had developed specific antibodies, although in a few this protective phenomenon did not occur. This has been shown also in certain British epidemics when more than one strain of virus is at work. To the clinician the main importance of this monograph is that the authors have made out a good case for the generally accepted theory that initial infection is by a specific virus, producing a characteristic mucosal lesion, following which, the secondary, more dangerous bacterial invasions may take place. Their concluding paragraph is therefore appropriate when they remind us that in every suspected case full use of prophylactic penicillin and the sulphonamides is justifiable, particularly when the nature of the bacteriology indicates that hæmolytic streptococcal or staphylococcal pneumonia is a possibility.

INFLUENZA AND ITS VIRUSES

By F. A. KNOTT, M.D., F.R.C.P., D.P.H.

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A RECENTLY published Dutch monograph* provides a useful summary of the present state of knowledge concerning the virus etiology of influenza, and is also a record of war-time study which does great credit to those who pursued it in face of many difficulties. Following the isolation of the bronchotropic influenza virus described by Smith, Laidlaw and Andrewes in 1933, workers at the Leyden institute were attracted to the subject, and ultimately a complete research team, meeting several times a year, was set up. As a result local information steadily accumulated until, by 1940, the stage was set for relatively complete investigation of the next epidemic. It came with the New Year and analysis of it is interesting. Before 1940 it was appreciated that viruses other than the Laidlaw strain must exist because virus A could be isolated in certain epidemics only. In that year Francis identified the B virus and later, subvariants came to light. The Laidlaw virus and its subvariants were thenceforward described as the A strain and that of Francis as the B.

As a prelude to their local studies the Dutch authors remind us that all observations on these A and B strains suggest that they are the cause of *inter*-pandemic influenza only. The true pandemics such as the world knew in 1889, starting in Turkestan in June, and in 1918, with a probable origin in Spain, and also beginning in June, show some clinical resemblance to the interpandemic disease. But there are certain essential differences. Outbreaks of the latter variety, studied since the virus A was known, have mainly been linked with the cold season and have occurred in several countries simultaneously without showing any steady spread over great distances. The incidence of complications is much higher in the pandemic form and the impression is gained that the pandemic virus is far more pneumotropic than are types A and B, which seem in main simply to reproduce in bronchotropic form the disease now so well known in experimental mice and ferrets. From the local outbreaks examined in Holland since 1933 it is clear that finding a sudden prevalence of either virus A or virus B does not mean that a great epidemic is about to begin. In 1935 interpandemic influenza arose from virus A; similarly in the winter 1936-37 and at Groningen in 1939 and 1941. In 1938 and 1943 also, influenza broke out but not due to A virus, and such evidence as can be collected blames the B strain.

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readers are referred to the reviews by Berry and Spies (1946), and by Cartwright (1947), and to the recent monograph by Spies (1947).

Synthetic folic acid has been tried in a wide variety of anæmias and other disorders of the blood, and the evidence is practically unanimous that it is hæmatopoietically effective only in the same broad group of anæmias in which liver therapy is also effective, namely, the megaloblastic anæmias. It will be recalled that this group comprises Addisonian pernicious anæmia, nutritional macrocytic anæmia, macrocytic anæmia associated with the sprue syndrome, megaloblastic anæmia of pregnancy, and certain rare megaloblastic anæmias of undetermined origin.

THE MEGALOBlastic ANÆMIAS

Although the megaloblastic nature of the erythropoiesis in such anæmias can only positively be established by the recognition of megaloblasts in sternal marrow films or occasionally in peripheral blood films, a provisional diagnosis may in many cases justifiably be based upon the peripheral blood picture and the clinical findings. It should be realized, however, that although megaloblastic erythropoiesis is usually associated with a macrocytic and hyperchromic blood picture, exceptions do occur. Thus, in pregnancy and nutritional deficiency, megaloblastic erythropoiesis may be associated with a hypochromic blood picture due to a concomitant iron deficiency, whereas, on the other hand, a macrocytic and hyperchromic blood picture may occasionally occur in conjunction with an essentially normoblastic bone marrow in conditions such as hæmolytic anæmia, aplastic anæmia, hepatic disease, scurvy, myxædema, and certain types of steatorrhæa. In the light of the available evidence it must be emphasized that no appreciable anti-anæmic effect can be expected from folic acid, or indeed from liver preparations, in any type of anæmia associated with normoblastic erythropoiesis, irrespective of the nature of the peripheral blood picture. It is necessary to point out, however, that this statement applies only to cases that have not recently received treatment with hæmatinics such as liver or folic acid. This is because the effective administration of these substances in a case of megaloblastic anæmia results in the prompt transformation of the marrow picture from a megaloblastic to a normoblastic one, and the subsequent cessation of adequate treatment may be followed by a lag period of weeks or months before the marrow picture once more becomes frankly megaloblastic, despite the existence of a subnormal blood count. The desirability of establishing a reasonably certain diagnosis before giving liver or folic acid will thus be evident. This problem has been fully discussed in a comprehensive review of the megaloblastic anæmias by Davidson and Davis (1947).

Effect on blood picture.—For the most part, all types of megaloblastic anæmia give an immediate hæmatopoietic response to folic acid similar to that obtained in comparable cases with effective liver therapy. There is a prompt reticulocyte response proportional in degree to the severity of the anæmia, a progressive rise in the red cell count with a fall in the colour index

CURRENT THERAPEUTICS

I.—FOLIC ACID

By L. J. DAVIS, M.D., F.R.C.P., F.R.C.P.Ed., F.R.F.P.S.G., F.R.S.E.
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FOLIC acid, now available in this country in tablet form under the trade name of "folvite", is a yellow crystalline synthetic compound, of known molecular constitution, for which the name pteroylglutamic acid has been proposed. Its synthesis was first announced in 1945 (Angier *et al.*, 1945), but the name "folic acid" had been introduced four years earlier to designate a substance of unknown chemical constitution isolated from spinach leaves (Mitchell, Snell and Williams, 1941). This substance was found to be highly active in promoting the growth of certain lactic acid bacteria in synthetic media, in this respect resembling a substance, or substances, known as the *Lactobacillus casei* factor, which had recently been obtained from yeast, liver and other sources.

Since the *L. casei* factors obtained from various sources were found to possess similar physical and chemical properties to the substances isolated from spinach leaves, the term folic acid, or folic acids, was often employed generically at this time for substances providing an essential growth factor for lactic acid bacteria. It soon became apparent that this group of substances was closely related to, if not identical with, the vitamins M and Bc which had been found to be essential for adequate hæmatopoiesis in monkeys and chicks respectively. In 1945, as already mentioned, the synthesis of pteroylglutamic acid was achieved, and this was found to possess the biological properties mentioned above. This synthetic substance is apparently identical with certain crystalline preparations that have been isolated from liver, but its relationship with other naturally occurring folic acid-like substances is at present uncertain. It has been shown, however, that pteroylglutamic acid is widely distributed in foodstuffs in conjugated forms which are relatively inert biologically, but capable of liberating free active pteroylglutamic acid on being exposed to the action of conjugase, an enzyme present in the tissues. Readers desiring an adequate account of the intriguing chain of researches which led to the discovery of folic acid are referred to the review by Berry and Spies (1946).

THE THERAPEUTIC ACTIVITY OF FOLIC ACID

When synthetic folic acid became available and its administration in relatively large doses was thus rendered practicable, evidence was soon produced of its activity in stimulating erythropoiesis in certain types of anæmia. Since it is scarcely feasible in this article to discuss in detail the already extensive literature dealing with the clinical aspects of folic acid,

while being treated with folic acid. In all these cases neurological improvement occurred when folic acid therapy was replaced by injections of refined liver extract. Spies and Stone (1947), Meyer (1947), Davidson and Girdwood (1947), and Wilkinson (1947) have had similar experiences.

In view of these findings, it is evident that folic acid should not be given as a substitute for liver products in the maintenance treatment of Addisonian pernicious anæmia. The suggestion that liver therapy be supplemented by folic acid should also be deprecated, except as a temporary measure, because this form of treatment might well result in the maintenance of a normal blood picture while the patient is receiving an inadequate dosage of the factor responsible for the preservation of the integrity of the nervous system.

Nutritional megaloblastic anæmia.—The first report of therapeutic success with synthetic folic acid by Spies and his colleagues was concerned with cases belonging to this category. Subsequent experience has indicated that the effect of folic acid in these cases is similar to that obtained with adequate liver therapy, both as regards the hæmatological and clinical responses. As with liver therapy, no subsequent maintenance treatment is necessary once a satisfactory remission has been obtained, provided the patient's previously faulty dietary habits are corrected. Serious neurological complications are extremely rare, and probably never occur subsequent to satisfactory therapeutic remission. The convenience of folic acid therapy may therefore justify its adoption as an alternative to liver therapy in this condition. Its use, however, must not lead to dietetic therapy being neglected. It is probably unnecessary to remark that nutritional megaloblastic anæmia is, as yet, an exceedingly rare condition in this country.

The sprue syndrome.—Shortly after the introduction of synthetic folic acid, success was claimed for it in the treatment of tropical sprue in Cuba, and of non-tropical sprue in the United States. Although further experience is necessary before folic acid can be evaluated adequately in the treatment of the sprue syndrome, the existing literature indicates that the hæmatological response depends upon the type of erythropoiesis present.

Patients suffering from the sprue syndrome may be classified into two broad groups. The first group comprises those with a severe macrocytic anæmia and with a frankly megaloblastic bone marrow picture. This is commonly seen in untreated, or inadequately treated, cases of tropical sprue in relapse, occasionally in non-tropical sprue in adults, and rarely in celiac disease in children. The patients successfully treated with folic acid by Spies and his colleagues in Cuba belonged to this group, although it should be noted that these patients had subsisted for long periods on diets defective in animal protein.

Spies emphasizes that in addition to a prompt hæmatological response, a rapid symptomatic improvement followed the institution of folic acid therapy. The appetite improved and soreness of the mouth and tongue disappeared, the diarrhœa usually ceased, the stools became normal in character, and the radiological appearances of the alimentary tract reverted to normality. A number of patients were

towards normality, and a rise in the white cell and platelet counts if previously depressed. The bone marrow picture becomes normoblastic, and the patient undergoes symptomatic improvement.

Dosage and method of administration.—The dosage employed has varied within wide limits. An optimal hæmatopoietic response has been obtained with as little as 1 mgm. daily, whilst 500 mgm. daily has been given without undesirable effects. Manifestations of sensitivity have not been recorded, even in patients exhibiting sensitivity reactions to liver extracts. Folic acid may be given by mouth, intramuscularly or intravenously. An unexpected finding is that, in general, equivalent doses are equally effective whether given orally or parenterally. In this respect folic acid differs from liver extracts, which are 60 to 100 times more effective when given parenterally than when given in equivalent quantities by mouth. Patients probably show as much individual variation in their therapeutic requirements for folic acid as they do for liver products. It is consequently impossible to recommend a standard minimal dose, but in the majority of patients an optimal hæmatopoietic response may be expected from the administration of 10 mgm. daily by mouth. Parenteral administration is seldom necessary, but should it be desired, Spies (1947) recommends that the tablets be dissolved in slightly alkaline saline and the solution be sterilized by autoclaving.

Although there is abundant evidence that folic acid is effective in the initial treatment of megaloblastic anæmias, relatively few data are yet available concerning its efficacy in maintenance therapy. This question may perhaps most conveniently be considered in connexion with an evaluation of folic acid therapy in the various types of megaloblastic anæmia.

Addisonian pernicious anæmia.—In this condition the efficacy of maintenance treatment is obviously of paramount importance because of the irreversible nature of the disease, and because of the danger of neurological complications attending inadequate treatment. It is now generally recognized that these neural disturbances can be prevented or, if already present, arrested by adequate liver therapy. Before folic acid can be accepted as an alternative to liver products in the routine treatment of pernicious anæmia it is therefore essential to determine not only whether it will maintain a normal blood picture, but whether it will also prevent neurological and other complications.

The available evidence is far from reassuring. Although it has been reported that in some cases a normal blood picture was attained and maintained for periods of months, in others the blood picture deteriorated, or was only maintained satisfactorily by increasing the dose of folic acid (Vilter, Vilter and Spies, 1947). The effect of folic acid upon the nervous system was found (Vilter *et al.*, 1947) to be particularly disappointing. Several patients actually developed progressive subacute combined degeneration of the spinal cord while on maintenance folic acid therapy, despite increasing the dosage to as high as 500 mgm. daily, whilst other patients, already suffering from neurological manifestations, deteriorated

while being treated with folic acid. In all these cases neurological improvement occurred when folic acid therapy was replaced by injections of refined liver extract. Spies and Stone (1947), Meyer (1947), Davidson and Girdwood (1947), and Wilkinson (1947) have had similar experiences.

In view of these findings, it is evident that folic acid should not be given as a substitute for liver products in the maintenance treatment of Addisonian pernicious anæmia. The suggestion that liver therapy be supplemented by folic acid should also be deprecated, except as a temporary measure, because this form of treatment might well result in the maintenance of a normal blood picture while the patient is receiving an inadequate dosage of the factor responsible for the preservation of the integrity of the nervous system.

Nutritional megaloblastic anæmia.—The first report of therapeutic success with synthetic folic acid by Spies and his colleagues was concerned with cases belonging to this category. Subsequent experience has indicated that the effect of folic acid in these cases is similar to that obtained with adequate liver therapy, both as regards the hæmatological and clinical responses. As with liver therapy, no subsequent maintenance treatment is necessary once a satisfactory remission has been obtained, provided the patient's previously faulty dietary habits are corrected. Serious neurological complications are extremely rare, and probably never occur subsequent to satisfactory therapeutic remission. The convenience of folic acid therapy may therefore justify its adoption as an alternative to liver therapy in this condition. Its use, however, must not lead to dietetic therapy being neglected. It is probably unnecessary to remark that nutritional megaloblastic anæmia is, as yet, an exceedingly rare condition in this country.

The sprue syndrome.—Shortly after the introduction of synthetic folic acid, success was claimed for it in the treatment of tropical sprue in Cuba, and of non-tropical sprue in the United States. Although further experience is necessary before folic acid can be evaluated adequately in the treatment of the sprue syndrome, the existing literature indicates that the hæmatological response depends upon the type of erythropoiesis present.

Patients suffering from the sprue syndrome may be classified into two broad groups. The first group comprises those with a severe macrocytic anæmia and with a frankly megaloblastic bone marrow picture. This is commonly seen in untreated, or inadequately treated, cases of tropical sprue in relapse, occasionally in non-tropical sprue in adults, and rarely in coeliac disease in children. The patients successfully treated with folic acid by Spies and his colleagues in Cuba belonged to this group, although it should be noted that these patients had subsisted for long periods on diets defective in animal protein.

Spies emphasizes that in addition to a prompt hæmatological response, a rapid symptomatic improvement followed the institution of folic acid therapy. The appetite improved and soreness of the mouth and tongue disappeared, the diarrhœa usually ceased, the stools became normal in character, and the radiological appearances of the alimentary tract reverted to normality. A number of patients were

towards normality, and a rise in the white cell and platelet counts if previously depressed. The bone marrow picture becomes normoblastic, and the patient undergoes symptomatic improvement.

Dosage and method of administration.—The dosage employed has varied within wide limits. An optimal hæmatopoietic response has been obtained with as little as 1 mgm. daily, whilst 500 mgm. daily has been given without undesirable effects. Manifestations of sensitivity have not been recorded, even in patients exhibiting sensitivity reactions to liver extracts. Folic acid may be given by mouth, intramuscularly or intravenously. An unexpected finding is that, in general, equivalent doses are equally effective whether given orally or parenterally. In this respect folic acid differs from liver extracts, which are 60 to 100 times more effective when given parenterally than when given in equivalent quantities by mouth. Patients probably show as much individual variation in their therapeutic requirements for folic acid as they do for liver products. It is consequently impossible to recommend a standard minimal dose, but in the majority of patients an optimal hæmatopoietic response may be expected from the administration of 10 mgm. daily by mouth. Parenteral administration is seldom necessary, but should it be desired, Spies (1947) recommends that the tablets be dissolved in slightly alkaline saline and the solution be sterilized by autoclaving.

Although there is abundant evidence that folic acid is effective in the initial treatment of megaloblastic anæmias, relatively few data are yet available concerning its efficacy in maintenance therapy. This question may perhaps most conveniently be considered in connexion with an evaluation of folic acid therapy in the various types of megaloblastic anæmia.

Addisonian pernicious anæmia.—In this condition the efficacy of maintenance treatment is obviously of paramount importance because of the irreversible nature of the disease, and because of the danger of neurological complications attending inadequate treatment. It is now generally recognized that these neural disturbances can be prevented or, if already present, arrested by adequate liver therapy. Before folic acid can be accepted as an alternative to liver products in the routine treatment of pernicious anæmia it is therefore essential to determine not only whether it will maintain a normal blood picture, but whether it will also prevent neurological and other complications.

The available evidence is far from reassuring. Although it has been reported that in some cases a normal blood picture was attained and maintained for periods of months, in others the blood picture deteriorated, or was only maintained satisfactorily by increasing the dose of folic acid (Vilter, Vilter and Spies, 1947). The effect of folic acid upon the nervous system was found (Vilter *et al.*, 1947) to be particularly disappointing. Several patients actually developed progressive subacute combined degeneration of the spinal cord while on maintenance folic acid therapy, despite increasing the dosage to as high as 500 mgm. daily, whilst other patients, already suffering from neurological manifestations, deteriorated

megaloblastic anæmias of pregnancy, since subsequent maintenance therapy is probably never necessary and neurological complications are unknown.

Refractory megaloblastic anæmias.—Attention has been drawn during recent years to cases of megaloblastic anæmia which are completely or partially refractory to injections of potent liver extract, and it has been shown that these cases will respond promptly to proteolysed liver or other liver preparations administered orally (Davis and Davidson, 1944; Fullerton, 1943; Davis and Brown, 1947). This phenomenon has been observed relatively frequently in the megaloblastic anæmias associated with sprue, pregnancy, and defective nutrition, and occasionally in apparent cases of Addisonian pernicious anæmia formerly responsive to parenteral liver.

Davidson and Girdwood (1946, 1947) have reported five cases, all of which responded initially to folic acid, but in none of them was the blood picture completely restored to normality with folic acid alone, although in two this was subsequently achieved by substituting proteolysed liver for folic acid. Davidson (1947) has, however, subsequently succeeded in securing a normal blood picture in other cases with folic acid alone. A patient with refractory nutritional megaloblastic anæmia under my care was restored to a normal blood count with folic acid, but only when the dosage was raised from 20 to 80 mgm. daily.

It would thus appear that although folic acid may be effective in restoring a normal blood picture in some cases of refractory megaloblastic anæmia, it is at present doubtful whether, even in large doses, it is always as effective as oral liver preparations. The convenience of folic acid certainly justifies its trial. If it does not result in the restoration of a normal blood picture, oral liver therapy should also be employed. Should permanent maintenance therapy prove necessary, it is recommended that, with a view to avoiding the risk of neurological complications, reliance should be placed upon oral liver therapy rather than upon folic acid. In refractory anæmias associated with the sprue syndrome, however, this risk is probably very remote.

OTHER PATHOLOGICAL CONDITIONS

The existing evidence justifies the conclusion that folic acid is ineffective in the treatment of anæmias associated with normoblastic erythropoiesis. It has been shown to be valueless in hypochromic, aplastic, and hæmolytic anæmias, and in leukæmias. Although it will correct the leucopenia and thrombocytopenia associated with megaloblastic anæmias, it was found by Davidson and Girdwood (1947) to be valueless in other types of leucopenia and thrombocytopenia, including those due to X-ray therapy. These observers also found it useless in ulcerative colitis.

THE CLINICAL VALUE OF FOLIC ACID

Comparing the relative merits of folic acid and liver preparations from the point of view of practical therapeutics, it will be seen that folic acid has the following *advantages*:—

(1) Its administration is convenient, since it merely entails the ingestion of one or more small tablets.

completely restored to health, but in others the red cell count remained below normal.

Davidson (1947) has also treated cases belonging to this group with excellent symptomatic and hæmatological results. Some of these cases had previously failed to respond to parenteral liver therapy. In one such case, however, folic acid failed to restore the blood picture to normal, although this was subsequently effected by oral liver therapy.

The second group consists of cases of steatorrhœa associated with a normoblastic bone marrow picture. Anæmia, variable in degree, is usually present but is seldom so severe as in the first group. The blood picture may be macrocytic, normocytic, or microcytic. This state of affairs, which may be seen in the more chronic types of tropical sprue, especially in those patients who have received treatment, is commonly present in non-tropical sprue, and is usual in cœliac disease. The results of folic acid in this group appear to be less striking than in the megaloblastic group.

In a series of cases reported by Davidson, Girdwood and Innes (1947), the hæmatological response was disappointing, fat absorption studies revealed no significant improvement, but rapid amelioration of the symptoms, including diarrhœa and trophic manifestations, occurred in the adult patients, although no such benefit was observed in the three children with cœliac disease. The effect of folic acid in a number of chronic cases of the sprue syndrome with slight anæmia and normoblastic erythropoiesis has also been studied by me in conjunction with Dr. J. W. Ferguson. Hæmatological and fat balance studies revealed no significant improvement, but a varying degree of symptomatic improvement occurred, and radiology showed that in some cases abnormalities in the small intestinal pattern seen before treatment disappeared after the administration of folic acid.

From the available information it would appear that, in the treatment of the sprue syndrome in general, folic acid is usually as active as liver preparations, parenteral or oral, in promoting hæmatopoiesis, and that it is more effective in ameliorating gastro-intestinal symptoms. Moreover, since it possesses the advantage over oral liver therapy of ease in administration and assimilation, it should be of particular value in patients suffering from severe alimentary disturbances in expediting their symptomatic recovery to the stage at which a satisfactory diet may be taken. It may therefore be concluded that folic acid deserves a paramount place in the treatment of the sprue syndrome. It should nevertheless be supplemented by the usual dietetic and symptomatic measures, and by proteolysed liver or oral liver extracts, especially if hæmatological response is unsatisfactory. The recommended dose of folic acid in the sprue syndrome is 10 to 20 mgm. daily.

Megaloblastic anæmia of pregnancy and the puerperium.—In the few cases treated with folic acid which have been reported the response has been satisfactory. It should be noted, however, that in this condition many cases are refractory to parenteral liver extracts (Davidson, Davis and Innes, 1942), although readily responsive to oral liver therapy (Fullerton, 1943; Davis and Davidson, 1944). If experience shows that folic acid is effective in such cases, it may well provide a convenient method of treatment in

its discovery, for this may well lead to the elucidation of the fundamental nature of the megaloblastic anæmias, and throw an entirely new light on hæmatopoiesis, as well as on other physiological mechanisms. The biological functions of folic acid are being intensively studied by several groups of investigators. For a review and discussion of recent work in this field readers are referred to a paper by Welch (1947), but it may not be out of place here to mention some of the ideas that are receiving consideration.

For a number of reasons it is believed that neither folic acid nor its conjugates are identical in constitution, or in function, with the extrinsic factor, intrinsic factor, or with the anti-pernicious anæmia factor in liver extracts. It seems probable that folic acid acts as a vitamin in the synthesis of some of the materials required for hæmatopoiesis and other physiological activities. Active folic acid is normally derived by enzyme action from folic acid conjugates present in various foodstuffs. The defective hæmatopoiesis in pernicious anæmia is believed to result from a failure in, or an interference with, the utilization of the folic acid conjugates.

The functional relationship between folic acid and the active principle in liver extracts is obscure. Experimental evidence has led to the view that the active principle in liver extracts may exert its hæmatopoietic effect in pernicious anæmia by rectifying the failure in utilization of folic acid conjugates, but later observations have thrown considerable doubt on this hypothesis. In view, moreover, of the differences in the clinical effects of folic acid and refined liver extracts, such as the failure of folic acid to preserve the integrity of the nervous system, it seems likely that the two agents are concerned with separate physiological mechanisms which, although overlapping functionally, cannot entirely replace each other.

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(2) It is available in known quantities of constant potency. There is no danger of overdosage, or of producing manifestations of toxicity, or sensitization.

(3) It is effective in certain cases of megaloblastic anæmia refractory to parenteral liver extracts, although it is doubtful whether in this respect it is always as effective as oral liver preparations.

(4) It is apparently superior to liver preparations in ameliorating certain alimentary symptoms in the sprue syndrome.

The outstanding *disadvantages* of folic acid are its failure to protect against the neurological complications of pernicious anæmia, and its high cost. I believe that the present retail price of folic acid in this country is 17s. 6d. for 25 tablets each containing 5 mgm. A daily dose of 10 mgm. would therefore cost 42s. a month compared with 5s. to 10s. a month for maintenance therapy with liver extracts. On the other hand, the cost of folic acid compares not unfavourably with that of oral liver preparations.

Summarizing the clinical applications of folic acid, it may be stated that in the light of available knowledge folic acid may be of value in the following circumstances:—

(1) In cases of Addisonian pernicious anæmia in which sensitivity to liver extracts has developed. It should be emphasized that this use of folic acid must be limited to a temporary period not exceeding a few weeks, and should not be regarded as a substitute for desensitization. In cases in which this procedure is not undertaken, permanent treatment should consist of the oral administration of liver products or of hog's stomach. The use of folic acid in Addisonian pernicious anæmia may also be justified for strictly limited periods when circumstances render the injections of liver extracts impracticable, as for example when travelling. It should be realized, however, that interruptions in parenteral liver therapy may lead to the development of sensitization.

(2) In cases of megaloblastic anæmia associated with defective nutrition, or pregnancy, which are refractory to parenteral liver therapy, folic acid may be preferable to oral liver preparations, especially if gastro-intestinal disturbances are present. If folic acid fails to restore the blood count to normality in such cases, it should be replaced or supplemented by proteolysed liver or oral liver extracts. In cases belonging to this etiological group, even if not refractory to parenteral liver, folic acid may be preferred on the score of convenience, if the expense is no objection.

(3) The sprue syndrome: It is in the treatment of this condition that folic acid will probably prove of most value. It should be used to supplement rather than to replace established therapeutic measures.

THE THEORETICAL SIGNIFICANCE OF FOLIC ACID

Although folic acid has at present only a limited field of usefulness in clinical medicine, it would be a mistake to underestimate the scientific importance of

years to be an increased tension in the posterior portion of the pelvic diaphragm and its associated ligamentous structures.

It is the acquired type of *retroversion* that may cause backache. It is less frequently due to the mobile acquired retroversion as seen in the post-partum patient than to the fixed type. The increased tension in the posterior segment of the pelvic diaphragm is slight or nonexistent in the mobile type and hence is unlikely to produce a reflex pain in the sacral area. At times, however, some tension does exist, especially at the time of menstruation, and low back pain results. In such patients position of the uterus and fixation by means of a pessary relieve the backache. Required retroversion of the fixed type is more often the cause of backache. This is probably due to an increased tension caused by the inflammatory process producing fixation, if still active, or to increased tension in pelvic peritoneal bands produced by gravity. Similarly, in *prolapse of the uterus*, gravity increases the tension in the posterior segment of the pelvic diaphragm with consequent referred backache. Patients in whom gravity appears to increase this tension often experience an associated dragging or bearing down sensation which is relieved when the effect of gravity is removed by lying down. In patients with prolapse the backache can be produced by pulling down the cervix towards the vaginal introitus.

Backache may be associated with *cervicitis* and *endometritis*. In such cases the inflammation has extended beyond the confines of the uterine wall to the pelvic cellular tissues to produce a cellulitis, and it is from the posterior segment of the pelvic cellular tissues that the referred backache arises. Similarly, in inflammatory conditions of the Fallopian tube and ovary it is an extension of the inflammatory process to the pelvic peritoneum and cellular tissues that is responsible for the backache. In the same way endometriosis affecting the posterior part of the pelvis may cause low back pain. Here the increased tension is the result of the cyclical changes which occur in the lesion itself. In these inflammatory conditions the patient will also complain of deep dyspareunia. The pain in the back tends to be relieved by rest and made worse by exertion, and is liable to exacerbation at the time of the period. There will be evidence of the original lesion and of the extension in the form of induration or altered position of the uterus. Pressure on the area of extended inflammation, if it can be reached, will reproduce the referred backache. It should be mentioned here that infective inflammatory lesions of the genital tract may constitute a focus of infection which has been incriminated by many authorities as the etiological factor in fibrositis and also spondylitis.

Neoplasms of the genital tract may be associated with backache. Ovarian tumours and fibroids of the uterus, when tightly impacted in the pelvis, produce a referred pain in the sacral area by the tension created in the posterior portion of the pelvis. This is analogous to the low back pain found in the later stage of labour, when the fetal head is stretching the posterior pelvic floor. Cancer of the uterus may be responsible for pain referred to the lower back. This is more commonly seen in carcinoma of the cervix and is due to its extension postero-laterally to involve the retro-sacral ligaments and pelvic floor, or to inflammation of these structures as a result of infection of the necrotic tumour. In carcinoma of the body of the uterus, extension into the pelvic floor is not so often seen and hence backache is not a common symptom. The pain due to malignant growth is not relieved by rest.

It should be remembered that a lesion of the genital tract may extend to involve the ureter and so produce back pressure on the kidney. This is more likely to occur with a neoplastic rather than with an inflammatory lesion. In such cases there is referred renal pain to the upper lumbar region of the back. Pain in the back above this level is not due to any gynaecological lesion. Rectal lesions may also be responsible for sacral pain. This may result from the lesion producing an increase

REVISION CORNER

BACKACHE IN WOMEN

ONE of the most common disabilities of women is backache in the lumbo-sacral region. Unfortunately there is too great a readiness, both on the part of the practitioner and patient, to conclude that this ailment is most likely to be due to some disorder of the pelvic organs. Especially is this so when the backache is worse at the time of the period. Nothing could be further from the truth, for the majority of cases are due to orthopædic causes.

ORTHOPÆDIC FACTORS

Postural strain may be a factor in some cases of backache. This often accompanies a bad stance adopted by the young woman in her late teens, or the debilitated woman after operation, severe illness or confinement. In its more severe form it accompanies kyphosis, lordosis, scoliosis or pregnancy. Backache due to this cause is relieved by rest, and is unaccompanied by restricted movement of the spine. Correction of the faulty posture cures the backache. Stiffness of the back muscles may result from unaccustomed exercise. This causes a backache which is worse on movement following a period of rest and which improves with further movement. The condition is temporary.

Low back pain may result from *sacro-iliac strain*, a rare lesion. In this condition the pain may be reproduced by compressing the iliac crests, and there may be palpable subluxation of the joint. In long-standing cases arthritic changes may be seen in the X-ray.

The term "fibrositis" has been used as a diagnostic label for many cases of low back pain when the exact cause has not been elucidated. In other words, it is the diagnosis when all other causes have been excluded. Fibrositis is said to cause pain which is improved by rest; it is associated with areas of induration, and results from focal infection, tonsillitis, influenza, changes of temperature, and dampness. With the passage of time and consequent increase in knowledge of the causes of backache, fewer cases are now diagnosed as fibrositis.

Some observers believe that the majority of cases of low backache of the chronic type are due to *intervertebral disc lesions*. Backache due to this cause is often associated with sciatica, especially when the backache is severe. There is localized tenderness due to muscle spasm, which has been attributed to irritation of a nerve root before it leaves the spinal canal, and there is some restriction of movement of the spine, notably flexion.

Other pathological conditions of the spine which may cause backache are osteoarthritis, spondylitis, spondylolisthesis, Paget's disease, osteomyelitis and neoplasms. Such conditions can be excluded quite readily by examination and X-rays. It should be mentioned that backache due to such orthopædic causes may be worse at the time of menstruation. It is possible that this is due to slight relaxation of ligamentous structures associated with the hormone changes at this time.

BACKACHE OF GENITAL ORIGIN

Backache may be due to *abnormalities of the female genital organs*. Here the pain is referred to the sacral and lower lumbar region of the spine. There may be tenderness which is localized and constant. Examination of the spine shows no restricted movement. Such pain may be due to retroversion; prolapse of the uterus; inflammation of the uterus, its appendages, pelvic cellular tissue or pelvic peritoneum; and neoplasms of the uterus or its appendages. The common factor in all these conditions

The pupil reactions and ankle jerks must be examined to exclude tabes and other neurological causes. The tongue and temperature will give a hint of associated renal damage and infection which may be confirmed by past or present epididymitis. The bladder swelling is hard and tender in genuine acute retention, but in some cases of acute retention superimposed on chronic it is thinner and feels softer, and may have fallen towards one or other iliac fossa.

The *rectal examination* is important and may be misleading, unless it is borne in mind that the full bladder may push down the prostate gland to lie nearly transversely across the rectum, giving the sensation of considerable enlargement to inexperienced digital examination. Conversely, in acute retention a gland not feeling enlarged may be accepted as normal, apart from the possibility of middle lobe enlargement and fibrosis. Consistency of the gland, however, is important in suggesting carcinoma or stone, lack of definition of the edge being in favour of carcinoma as would be a history of a sciatic type of pain and unilateral leg œdema. Urethral discharge may be present from prostatic stones, so that a rectal examination should be done for acute retention in such cases before diagnosing urethritis alone as the cause.

Examination of the penis and urethra will reveal stricture of the meatus, neoplasm, and stone or foreign body in the lumen.

X-ray examination.—An X-ray of the prostate and pelvis is often valuable to confirm the presence of stones or metastases.

TREATMENT

A hot bath (with specific instructions to the patient to void urine in the bath; a point of importance with some sensitive patients, even with retention) and an enema are worthy of trial in cases due to urethritis and in postoperative cases, although in the second group the bath is often not feasible; they may also be tried in prostatic obstruction while arrangements for admission are being made.

Carbachol and doryl are contraindicated for cases of mechanical obstruction such as stricture and prostatic retention, but are likely to prove useful in tabes and postoperative retention. Particular care should be given to instruction in dosage: 0.5 c.cm. of solution ($\frac{1}{8}$ mgm.).

If *carcinoma of the prostate* is definitely diagnosed catheterization may be carried out, as probably micturition will soon be re-established with stilbœstrol, 5 mgm. t.d.s. The catheter is removed on the 7th day to discover whether the patient can micturate; if he fails, a second week usually suffices and he may be admitted more leisurely to hospital for subcapsular orchidectomy which will allow the stilbœstrol dosage to be reduced to 1 mgm. t.d.s. This reduction of dosage delays the onset of stilbœstrol resistance. In cases of doubt stilbœstrol should not be given without a second opinion as a hard gland is quickly rendered soft and this may lead to faulty diagnosis.

Stricture and prostatic stones require the passage of a metal sound under local anaesthesia (0.1 per cent. amethocaine is satisfactory) and if this fails a filiform guide (gum elastic, sterilized in formalin vapour or by soaking for half an hour in biniodide of mercury; boiling makes them very soft) may be passed and Harrison's follow-on bougie attached or a Phillip's catheter, care being taken that the filiform has really passed the stricture and is not just buckling up in the urethra and so allowing the follow-on to make a dangerous false passage. The removal of the bougie should allow the patient to micturate and later to attend for regular dilatation. In the case of very "tough" strictures when the follow-on has failed it may suffice to tie in the filiform for twenty-four hours, allowing urine to trickle around and at the same time to soften the stricture and so facilitate later "bouginae".

Intermittent catheterization may be required after failure of simple remedies in

of tension in the posterior segment of the pelvic floor to give a referred pain, or to direct involvement of the sacrum itself.

CONCLUSION

An attempt has been made to show that pelvic lesions may produce backache in the lumbo-sacral area by causing an increase in tension in the posterior segment of the pelvic floor. It must be emphasized, however, that such lesions may exist without producing such an increase in tension and in such cases are not the cause of an accompanying backache. It is the lack of appreciation of this that accounts for so many patients having their backache attributed to a pelvic lesion whereas it is in fact due to an undiagnosed orthopædic cause. In order to treat the woman with this disabling symptom we must first determine which of the many causes is responsible for the symptom in her particular case. This requires full examination of the spine, including X-ray, and of the pelvis, and very often the help of the orthopædic surgeon or physiotherapist.

H. H. FOURACRE BARNS, F.R.C.S., M.R.C.O.G.

THE TREATMENT OF RETENTION OF URINE

IN the management of retention of urine in general practice much depends upon the diagnosis of the cause, and a rough classification is given here.

- (1) Prostate—Simple enlargement
Carcinoma
Fibrosis, with or without stones
Prostatitis, and abscess
- (2) Urethral stricture
- (3) Urethritis
- (4) Nervous diseases, e.g. tabes
- (5) Trauma: spinal injury, ruptured urethra
- (6) Postoperative, post-parturition
- (7) Rarer causes: pelvic tumours, including pregnancy; stone; growth or foreign body in or around the urethra; senile atonic bladder; hysteria

Infection remains the most serious complication in treating these cases, even attendant uræmia being in the majority of cases purely the result of pyelonephritis. The infection is commonly introduced by urethral instrumentation, which should be withheld if possible, particularly in patients for whom admission to hospital is essential. The best example of this type is the paralysed bladder of spinal injury when the distention and retention are complete, but no attempts must be made to relieve this; the patient may safely have his bladder ignored for two or three days until his arrival in a hospital specializing in spinal injuries. Similarly, with a ruptured urethra hospital treatment is necessary, but the pain of the full bladder should be relieved by morphine rather than by an attempt to catheterize. If the pain is unbearable a lumbar puncture needle introduced above the symphysis pubis will give relief with less risk of infection during the period of the patient's transfer to hospital.

DIAGNOSIS

In the diagnosis of the cause of acute retention it is necessary to exclude suppression of urine, an example being one patient who had the daily passage of a bougie for a supposed stricture when in reality a stone was lodged at the lower end of each ureter.

Previous history of Neisserian infection (often more than forty years ago) and some recent straining micturition and increasing poverty of the stream will suggest stricture. In other cases nocturnal frequency, hesitancy, urgency and the necessity for avoiding straining will indicate prostatic obstruction, although in some cases an acute retention must be numbered as the first symptom of such an enlargement.

washed out daily (1:8000 oxycyanide of mercury being favoured) and attention given to ensure satisfactory working of the catheter, which should be connected to a clear-glass bedside bottle, regularly inspected and emptied. The meatus should be cleaned daily and the whole wrapped in an antiseptic swab. The patient should be allowed up so far as possible (with the bottle at the chair side and not spigotted) and should be taught breathing exercises.

In some cases of acute retention with uræmia and pyelonephritis, intravenous saline or sodium sulphate may be needed. Glucose, 20 c.cm. of a 50 per cent. solution, is a valuable diuretic, but must be given rapidly intravenously and followed by saline, otherwise clotting will occur. Suprapubic cystotomy is now mainly reserved for (a) patients who cannot tolerate a catheter; (b) cases of great mechanical difficulty in passing an instrument. Intermittent catheterization in simple prostatic retention is justified only when there have been no previous symptoms and there is some hope that by relief of the overdistended bladder micturition may be re-established and allow operative treatment to be carried out in a quiet and clean interval. When the retention is due to *blood clot*, evacuation is best carried out under anæsthesia with a Bigelow's evacuator; this allows cystoscopic examination to be done and in some cases cauterization of the bleeding point.

In conclusion, it is well to stress again the importance of avoiding infection; intravenous hexamine, 5 c.cm. b.d.s., is a useful therapeutic agent for this purpose if the recommended penicillin and sulphonamide therapy are for any reason not feasible.

J. G. YATES BELL, M.B., F.R.C.S.

NOTES AND QUERIES

Subscribers are invited to make use of the service provided in this section. Answers from experts will be obtained and dispatched as soon as possible to the senders of the queries. Publication of selected and suitable queries and replies is arranged according to available space.

Alcohol and Pregnancy

QUERY.—There appears to be a fairly widespread view held among laymen that alcohol should not be taken during pregnancy, but expert views differ. Is danger to the mother's health implied, or danger to the growing foetus? In either event, what pathological changes would be expected to take place in the maternal or foetal organism as a result of moderate alcohol intake?

REPLY.—If a woman is in the habit of taking alcohol in ordinary moderation it is difficult to see how it can do any harm during pregnancy, provided that she does not suffer unduly from heartburn. In some cases when gastric digestion is sluggish a small amount of alcohol with food, or crème de menthe after a meal may be of considerable benefit. Experience of pregnant women and their varying habits does not indicate that moderate alcohol has the slightest discernible harmful effect on the foetus.

ALECK W. BOURNE, F.R.C.S., F.R.C.O.G.

Calciferol in the Treatment of Chilblains

QUERY.—What is the value of calciferol in the prophylactic or therapeutic treatment of chilblains? What is the most suitable preparation,

mode of administration and scheme of dosage? Is pregnancy a contraindication to its use?

REPLY.—The published results of the value of calciferol in the prophylaxis or treatment of chilblains have been very conflicting. My own experiences have led me to the conclusion that it is well worth a trial. It can be given by mouth as the high potency "ostelin" (Glaxo) tablet, each of which contain 50,000 units of vitamin D₂, or as "sterogyl" (Roussel), which is put up in either oily or alcoholic solution, in ampoules containing 600,000 units. The high potency ostelin tablets are given three times a day and the sterogyl ampoules once a week. It is necessary to watch carefully for symptoms of intoxication, e.g. thirst, nausea, vomiting, headache, as well as to have the serum calcium and serum alkaline phosphatase estimated at regular intervals. A drop in the serum alkaline phosphatase, which almost invariably precedes a rise in the serum calcium, is an indication for reducing the dose or withholding it.

Pregnancy, whilst not a complete contraindication, should indicate more care in the use, as the extra calcium taken in the form of milk and such like may increase the tendency to cause calcium deposits.

J. E. M. WIGLEY, M.D., F.R.C.P.

postoperative cases, and in infected cases with spasm, such as urethritis and prostatic abscess, combined with treatment for the infection, but there is a risk of causing epididymitis. As a general rule a tied-in catheter is less likely to cause infection than repeated passage of an instrument through an infected passage into a cavity likely to form a residual urine for bacteria to flourish in.

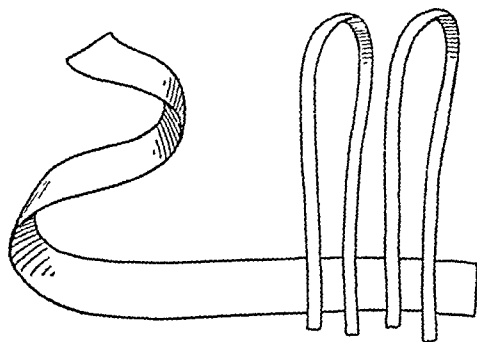


FIG. 1.—Loops of tape are first fixed to the adhesive side of the Elastoplast.

readily available), and 18 French the best size. It can be sterilized by boiling, and after passing it should be tied in with tapes and elastoplast (fig. 1-4) and the bladder

In retention from simple *prostatic enlargement*, infection is now the only serious problem and is almost invariably the result of catheterization, cystoscopy, or suprapubic cystotomy; with careful attention in hospital, infection can be avoided in the majority of cases. Preferably then, the patient should be admitted to hospital without catheterization and morphine should not be withheld during the few hours' wait. A Tieman's rubber catheter is the best for these cases (the Foley is ideal but not yet

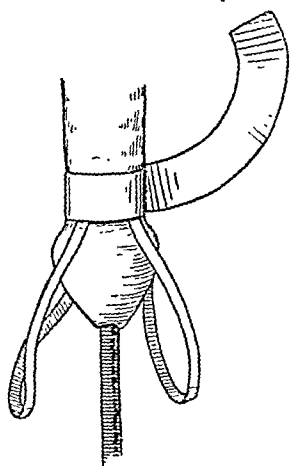


FIG. 2.—Elastoplast fixed to penis.

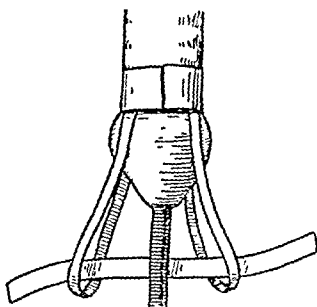


FIG. 3.—Fixing the tapes to the catheter with another piece of adhesive plaster, this allows adjustment of the catheter without removal of tapes and strapping from the penis.

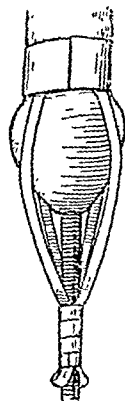


FIG. 4.—Tying-in is complete (for clarity the tapes are shown fixed somewhat farther from the meatus than is the usual practice).

emptied through an intravenous drip in about one hour; too rapid emptying may cause bleeding but very slow decompression is not now considered necessary.

All patients with an indwelling catheter are given penicillin, 200,000 units eight-hourly, until the catheter is removed after the operation, and this is supplemented by sulphadiazine if pyrexia develops. With this treatment, attention to fibrillating hearts, bronchitis and so on is possible without the infliction of a suprapubic cystotomy with its high morbidity and mortality rates, and the patient will be fit for a one-stage operation without an increase in the operation mortality rate. The bladder should be

with. At the induction, 400-600 c.cm. of air is probably sufficient. This can be gradually increased and the refills quickly spaced out to once a week with 1000-1200 c.cm. of air each time. It is necessary to control the height of the diaphragm by frequent "screening". Some physicians apply an abdominal binder during the early weeks of pneumoperitoneum treatment; others prefer to enhance the tone of the abdominal muscles by physical measures.

N. LLOYD RUSBY, D.M., M.R.C.P.

Vitamin E in Dupuytren's Contracture

QUERY.—I read in the October 1947 issue (p.

253) that Dupuytren's contracture may be treated with large doses of vitamin E. Could you let me know the dosage used, duration of treatment, and if any ill-effects were reported in any of the cases treated?

REPLY.—We are treating some cases in this clinic with the large doses of vitamin E advocated and are prescribing this in the form of "ephynal" (Roche), 100 mgm. per day, by mouth. It is too early yet to comment on results, and I am not aware of any ill-effects.

Professor LAMBERT ROGERS, M.Sc., F.R.C.S.

PRACTICAL NOTES

Penicillin in Streptococcal Carriers

IN a series of 18 chronic carriers of beta-hæmolytic streptococci among children who had had rheumatic fever, J. R. Goerner *et al.* (*New England Journal of Medicine*, October 16, 1947, 237, 576) found that the intramuscular administration of penicillin eliminated the infecting organism from the throat in 15 cases. A similar result was obtained in two cases of acute streptococcal tonsillitis. The dosage of penicillin was 10,000 units every two hours, day and night, for ten days. In five of the patients tonsillectomy was performed 125 to 185 days after treatment, and it was then found that the tonsils and tonsillar fossæ were free from hæmolytic streptococci. A further series of six children received penicillin in beeswax and peanut oil—single daily intramuscular injections of 150,000 units for ten days. In five of these children, all of whom were chronic beta-hæmolytic streptococcal carriers, the infecting organism was eliminated. It is concluded that "the ability to eliminate beta-hæmolytic streptococci from the throats of most patients in close contact with persons who have had rheumatic fever suggests a practical method of protecting the latter group from beta-hæmolytic streptococcus infection". It is also suggested that "it is evident that further observations are needed to ascertain whether prompt penicillin treatment for acute hæmolytic streptococcus infections in subjects with rheumatic fever may decrease the likelihood of a recurrence of rheumatic fever".

A Method for Prolonging the Action of Penicillin

A SIMPLE method for prolonging the action of penicillin and maintaining a satisfactory concentration in the blood, which is stated to produce results equal to those obtained by injections of oily solutions, is described by

E. Carlinfanti and F. Morra (*Schweizerische Medizinische Wochenschrift*, November 22, 1947, 77, 1235). The penicillin is injected by subcutaneous route into the thigh or arm after the circulation of the injection area has been retarded by the application of a rubber tourniquet, using a pressure slightly less than the minimal arterial pressure. The tourniquet must not be left in place for more than one to five hours, according to the amount of penicillin injected, i.e. 10,000 to 100,000 units. Using this method the number of injections can be reduced to three of 75,000 units in twenty-four hours, or five of 100,000 units in forty-eight hours, or the quantity of penicillin injected may be reduced to 80,000 units, giving eight injections of 10,000 units in twenty-four hours. It is probable that with doses of 600,000 to 800,000 units that a single injection might suffice to maintain a satisfactory penicillin concentration in the blood for twenty-four hours. Accompanying graphs show that after injection of 16,000 units the blood concentration level was maintained for four hours, the tourniquet being removed 1½ hours after injection; after injection of 75,000 units it was maintained for 8½ hours, the tourniquet being removed after 3½ hours, and after injection of 100,000, the level was maintained for 8½ hours, these levels being in comparison with 2½, 4½ and 6 hours blood level concentration when no tourniquet was used. The pressure exerted by the tourniquet must be regulated by the absence of painful sensations in the limb. It is stated that with the use of this method the number of injections can be reduced and at the same time a considerable economy in penicillin usage can be effected.

Sodium Ascorbate and Allergic Conditions

AMERICAN workers have for some time been recommending large doses of vitamin C (1000 to

Myasthenia Gravis or Hysteria?

QUERY.—A female patient, aged sixty years, has to my knowledge had an essential hypertension (280/130) for the last eight years. For the past four months she finds her eyelids keep closing, so that now she spends the entire day opening her lids. There is no weakness of the muscle, or any other muscles in her body. One month ago she saw an ophthalmologist, who considered her eyes perfect, but made no suggestion about the difficulty of keeping her eyelids open. Apart from this disability she feels quite well. Can you suggest any etiology, or treatment?

REPLY.—In the absence of any associated cranial nerve paresis or other neurological signs, the diagnosis lies between myasthenia gravis and hysteria. The former will be proved by the condition being less, or even absent, first thing in the morning, and by a therapeutic test of an injection of prostigmin methyl sulphate 1.5 mgm., and atropine sulphate 1/100 grain (0.65 mgm.); improvement occurs within twenty minutes of the injection. If myasthenia is proved the treatment will be prostigmin, 5 mgm. t.d.s. by the mouth, or ephedrine, $\frac{1}{2}$ grain (32 mgm.) t.d.s., or eserine, 1/12 grain (5.4 mgm.) t.d.s. If the condition is hysterical, the method of treatment must be left to the doctor in charge of the case who knows the patient and all the circumstances of the condition.

HECTOR K. GOADBY, M.D., F.R.C.P.

Depersonalization

QUERY.—A married childless woman of forty-eight years of age with physical menopausal symptoms, developed a melancholia, the onset of which appeared to coincide with the administration of nitrous oxide for dental extraction. Previous medical history, apart from a nervous breakdown at twenty-three years, is inconsequent and trivial. Electro-convulsive treatment (nine times) improved the melancholia and she appeared to recover expression in her face, but one symptom, that of "depersonalization"—a feeling that she is not herself—has persisted and remained intractable. Benzodrine and allied drugs have had no effect, nor have phenobarbitone and œstrin. Do you consider that intravenous narcosis with suggestion might help to remove the veil that is separating "herself from herself"? Could it do any harm apart from giving her an anæsthetic dose, if not any good? And what of the prognosis?

REPLY.—There are both psychological and physical factors in the causation of depersonalization. Since it is possible for the patient by worrying to magnify the symptoms, the treatment suggested may cause considerable

benefit and can do no harm. However, physical factors can also be important in its causation. It has been artificially produced by mescalin, and it may result from great fatigue. In the present case the biochemical changes at the menopause are probably the main factor in its causation, and the patient, now that she has lost her depression, should be reassured that depersonalization will disappear in time.

A. SPENCER PATERSON, M.D., F.R.C.P.E.

The Induction and Refills of Pneumoperitoneum

QUERY.—I have been unable to find in any standard textbook on tuberculosis the correct technique for induction and refills of pneumoperitoneum (a) in the usual site—left side of abdomen; (b) through the right side of diaphragm.

REPLY.—There is a choice of three sites for induction of pneumoperitoneum: (1) an inch or two below the umbilicus, either in the midline or lateral to the rectus muscle; (2) a short distance below the left costal margin, also lateral to the rectus muscle; and (3) through one of the lower right intercostal spaces in the mid-axillary line. The last carries with it the danger of injuring the liver. If the subumbilical route is used the bladder should first be emptied.

The technique is not difficult for anyone familiar with pneumothorax work: the same induction needle and apparatus can be used. After preliminary sterilization the skin is anaesthetized and anaesthesia continued through the abdominal wall to the peritoneum. A small nick is made in the skin through which the induction needle can easily pass and this is inserted through the abdominal wall with the sharp stylet. A blunt stylet may be used to perforate the peritoneum. The passage of the needle is greatly helped if the patient is asked to raise the head and shoulders slightly off the pillow; this tautens the abdominal muscles and counteracts sagging. It is not always easy to know when the peritoneal cavity has been reached as the pressure is not so readily registered as in the case of a pneumothorax. Often the perforation of the peritoneum can be felt. If not, the patient should be asked to cough gently and a free quick oscillation of the column of fluid in the manometer is seen if the needle is in the peritoneal space.

Refills can be given regularly under the left costal margin, or through one of the lower rib spaces, choosing, for preference, the side on which the diaphragm is paralysed if a phrenic operation has been done. If a thin sharp-ended pneumothorax refill needle of the Morland pattern is used local anaesthesia can be dispensed

The Removal of Cutaneous Stains

THE successful removal of cutaneous stains, such as those caused by potassium permanganate or gentian violet, by the use of depilatories which contain alkaline sulphides is recorded by T. Cornbleet (*Journal of the American Medical Association*, November 1, 1947, 135, 573). When a depilatory is applied for the removal of hair, if the procedure is carried out properly, the product also removes the outermost layer of the epidermis without causing irritation. If applied solely for the removal of stains on the skin the application need not be so long and there is even less possibility of any skin irritation occurring. Thus it is stated that the chemical depilatories "neet" and "sleek" require about five minutes to remove stains from the skin; to clean the nails the application needs to be a little longer. For removal of stains from the hair, a dilute solution of a sulphide, such as the calcium salt, is recommended to be applied for extremely short intervals followed by rinsing, the procedure being repeated until the desired effect is obtained. In this connexion, however, it is stated that "great care and some experience are needed to remove the stains and to leave the hair intact". The author has also used the method for the removal of adherent scales and crusts which persist some time after a dermatitis has disappeared, and for the removal of discoloration following medicinal applications after complete healing of the lesions, but pigmentary stains of the skin, such as those which follow an inflammation, are too deeply imbedded for removal by the method.

Folic Acid and Purpura

Two cases of thrombocytopenic purpura in which the administration of folic acid appeared to be of value are reported by T. H. Gridley and T. R. Waugh (*Canadian Medical Association Journal*, November 1947, 57, 487). One was a woman, aged fifty-two years, in whom splenectomy had been performed for the condition in 1943. This was followed by only temporary improvement. During the next three years various forms of treatment were tried, including blood transfusions, vitamin C, vitamin K, snake venom, and so forth, but all without avail. In May 1946, during a particularly severe attack of purpura, she was given folic acid orally in daily doses of 10 mgm. Improvement was noted on the sixth day. When last seen, fourteen months later, "she had no signs or symptoms of a recurrence of the hæmorrhagic diathesis". The second case was one of purpura due to bismuth

intoxication in a man aged sixty-six years. Folic acid was given orally in daily doses of 5 mgm., with some improvement, but it was not until the daily dose was increased to 10 mgm. that the purpuric eruption disappeared completely. Four months later the patient was still taking folic acid and there had been no recurrence of the purpura.

Vitamin B₁ and Gynergen in the Treatment of Herpes Zoster

A COMBINED therapy of vitamin B₁ and gynergen has been used with success by F. Lana Martínez and J. L. Lana Salarrullana (*Medicina Española*, July 1947, 18, 136) in a series of cases of herpes zoster. The recommended dosage of vitamin B₁ is 2, 5 or 10 mgm. daily, by subcutaneous or intravenous injection, and of gynergen 0.5, 1 and 1.5 c.cm. by subcutaneous injection. In some cases higher dosage was used, as in the case of a seventy-year old patient who after receiving 10 mgm. vitamin B₁ and 2 c.cm. gynergen for the first three days was given 20 mgm. vitamin B₁ and 2 c.cm. gynergen for the following three days, with resultant complete disappearance of pain. In another case, that of a thirty-year old man with extensive eruption, fever, and severe lumbago, 1 c.cm. gynergen and 10 mgm. vitamin B₁ were given for the first three days; on the fourth day there was complete disappearance of fever and lumbago, the vesicles began to dry and the scabs fell off on the twelfth day. No other analgesics were employed in any of the cases during the period of vitamin B₁ and gynergen therapy. There was no incidence of untoward secondary reactions apart from slight nausea and vomiting and sensation of cold in the lower extremities in some cases following gynergen administration.

A Vehicle for Unpleasant Drugs

ACCORDING to the *Journal of the American Pharmaceutical Association* (May 1947, 8, 286) the following is the formula of "a neutral vehicle and digestive" which is being recommended by the Joint Committee on Professional Relations of the Medical Society of New Jersey and the New Jersey Pharmaceutical Association:—

Elixir Papain and Disatase	
Papain	1.8 gm.
Diastase	1.8 gm.
Glycerin	36.0 c.cm.
Alcohol	21.6 c.cm.
Water q.s.	120.0 c.cm.
Flavoured with compound spirit of orange; coloured red with solution amaranth.	

This preparation is said to produce no incompatibilities with carbonate or other alkaline salts and to be compatible with most other drugs.

2000 mgm. daily) in the treatment of refractory cases of allergy. On the basis of the fact that suprarenalectomized animals develop an increased sensitivity to histamine, S. L. Ruskin (*American Journal of Digestive Diseases*, September 1947, 14, 302) has investigated the value of the sodium salt of ascorbic acid (sodium ascorbate) in the treatment of refractory cases of allergy. Sodium ascorbate was given orally in the form of tablets, each containing 100 mgm. The dosage ranged from 3 to 5 tablets thrice daily. Details are given of eight patients treated in this way: five with hay fever, two with asthma, and one with "nasal allergy". All responded satisfactorily, and it is claimed that sodium ascorbate was more effective than ascorbic acid and "represents a marked advance in the therapeutic approach to allergy".

Vitamin K in the Treatment of Chilblains

USING a commercial preparation of acetomenaphthone, synthetic vitamin K, in an average dosage of 20 mgm. daily, the dosage varying, however, with the individual patient, D. P. Wheatley (*British Medical Journal*, November 1, 1947, ii, 689) has treated a small series of cases of chilblains. In one case, a man of thirty-seven with chilblains on the hands and feet and signs of ulceration of several toes, a single intramuscular injection of 5 mgm. acetomenaphthone was given. When seen one week later the fingers were normal and the toes showed only a slight residual swelling. A course of 10 mgm. acetomenaphthone twice daily by mouth was instituted, and by the end of a further week all signs of the chilblains had disappeared. There was no recurrence at the end of two months, during which time the man had resumed his outdoor work. Another patient who had mild chilblains in cold weather was given an oral course of 20 mgm. vitamin K daily. After five days the chilblains had disappeared. During a spell of severe weather shortly afterwards, 20 mgm. twice daily did not prevent the appearance of chilblains, but increase of dosage to 20 mgm. thrice daily resulted in their subsidence. A maintenance dose of 10 mgm. daily proved insufficient to prevent recurrence, but on institution of larger dosage which was continued for five weeks no further symptoms were encountered. Of the eight cases recorded, complete relief was obtained in three.

Benadryl and the Common Cold

ACCORDING to J. M. Brewster (*United States Naval Medical Bulletin*, September-October

1947, 47, 210), benadryl "has proved to be the most satisfying single therapeutic agent for the treatment of the common cold". This conclusion is based upon a series of 100 cases, in 10 per cent. of which benadryl completely aborted the condition, whilst in 95 per cent. there was shortening of the course of the disease with marked subjective relief. In adults the dose was one 50-mgm. capsule; this was rarely repeated more than once in twenty-four hours and that at bedtime. The night dose was combined with 10 grains (0.65 gm.) of aspirin. For children under twelve years of age the dose was 10 to 25 mgm. The value of benadryl in the common cold is attributed to (a) inhibition of the serous discharge from the respiratory mucous membrane; (b) its sedative action; (c) inhibition of the cough reflex, especially in children—this is attributed to elimination of postnasal dripping; (d) prevention of herpes when the benadryl is taken immediately after the appearance of the initial itching wheal. To be effective, it is emphasized that benadryl must be taken immediately the first symptom of a cold is noted.

Calciferol in the Treatment of Lupus Vulgaris

AN interim report on the results of investigations in a series of twenty patients with severe lupus vulgaris undergoing treatment with calciferol at Morland Hall is given by D. R. Macrae (*British Journal of Dermatology and Syphilis*, October 1947, 59, 333). The average age of the patients was thirty-eight years, and the average number of years they had had the disease before coming to Morland Hall for treatment was nineteen. The calciferol employed was high potency ostelin, 7 patients receiving it by intramuscular injections of an oily solution and 13 by mouth, 7 in the form of oil in capsules and 6 in the form of emulsion. The dosage employed was 150,000 units daily by mouth, or 600,000 units twice weekly by injection. Blood counts, sedimentation rates and calcium estimations were done at monthly intervals, and also tuberculin skin reactions by intracutaneous injections of 0.1 c.cm. of 1:1000 and 1:10,000 tuberculin into the skin of the forearm fortnightly. After the first two or three weeks each patient looked decidedly worse; the lupus was more angry and swollen and in some cases ulcers broke down spontaneously. After three weeks' treatment improvement began, the lupus becoming flatter and finally fibrosis appearing and squeezing the lupus so that in many cases there was disappearance of active disease. As regards toxicity, 11 of the 20 patients showed toxic symptoms; treatment was continued in 7 cases and the toxic effects disappeared within a few days.

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This preparation is said to produce no incompatibilities with carbonate or other alkaline salts and to be compatible with most other drugs.

REVIEWS OF BOOKS

The Appendix. By R. J. McNEILL LOVE, M.S., F.R.C.S., F.A.C.S. London: H. K. Lewis & Co. Ltd., 1947. Pp. vi and 186. Figures 54. Price 12s. 6d.

MR. McNEILL LOVE has been known for some time as an authority on diseases of the appendix, and he has now given us the best book that has been written round this surgical trophy. Every chapter is interesting and informative, including the admirable short historical survey which forms the first. The succeeding chapters on etiology, diagnosis and differential diagnosis could not be bettered, for they are packed with experience and clinical wisdom. The chapters on treatment deal with appendicitis in all its aspects, including general peritonitis and complications such as burst abdomen. The illustrations are clear and well chosen. A surgeon reviewer will always find points of disagreement with a surgeon-author over a subject on which all surgeons consider themselves authorities. Mr. Love has been perhaps too generous in allotting space to topics which he admits are valueless, such as the Battle incision, ileus duplex, or the use of gas-gangrene serum in peritonitis, or even dangerous, as the treatment of ileus by purges; space that might have been used in explaining how to get a Miller-Abbott tube past the pylorus, or discussing the management of salt and protein balance in patients on intravenous therapy. He has one bee in his bonnet, the expectant treatment of appendicular abscess, which he allows to buzz for 10 per cent. of the book. This little manual is a really helpful addition to the literature of an important subject.

Obstetrics and Gynaecology. By C. SCOTT RUSSELL, M.B., F.R.C.S., M.R.C.O.G. London: Oxford University Press, 1947. Pp. viii and 214. Figures 21. Price 12s. 6d.

THIS little book is intended for ex-Service doctors returning to civilian practice who wish to freshen their knowledge of obstetrics and gynaecology and obtain an insight into some of the advances made in recent years. The printing is excellent and the illustrations are clear. The important aspects of antenatal care, labour and the puerperium of the normal case are concisely and clearly written. The more important abnormalities, including disorders of the newborn, are then dealt with in a well-balanced manner, and the last part of the book is concerned with gynaecological conditions. The author has managed to steer a steady course among the many conflicting views at present held, and gives much sound advice. In places, however,

there is perhaps a tendency to advocate too much interference, which might prove dangerous in his readers' hands. For example, he would appear to encourage the use of oxytocic drugs in the third stage of normal labour to aid delivery of the placenta. A normal third stage does not need such unnatural interference. Similarly, the wisdom of advocating the insertion of a vaginal pessary for retroversion and prolapse during the early days of involution and thereby stretching incompletely involuted tissues is questionable. In spite of this tendency the author is to be congratulated on this little book which should readily appeal to those for whom it is intended.

Rheumatism and Soft Tissue Injuries. By JAMES CYRIAX, M.D. London: Hamish Hamilton Medical Books, 1947. Pp. 410. Figures 101 and 107 plates. Price 42s.

THIS book is well produced and excellently illustrated. The detail with which Dr. Cyriax describes his methods of diagnosis, and in particular his manipulative and massage technique, is an example of clarity. Some of his theories of causation and etiology will not, however, be acceptable to all. His dogmatic statement that "lumbago . . . is now known to have no connexion with rheumatism, being in fact the name given to an attack of internal derangement in a low lumbar spinal joint" and that "the commonest cause of back-ache in all except the elderly is fragmentation of a low lumbar intervertebral disc" will certainly disturb many. He leans to the old "adhesion" theory of fibrositis, and while mentioning Elliott's theory of local muscle spasm he ignores Copeman's "fat" theory, stating that tender fatty nodules have nothing to do with rheumatism or fibrositis. The author is quite dogmatic that vaccines are valueless, but leans towards a virus etiology of the rheumatic group of diseases. He gives reasons for some of his theories and there are many suggestions that make one think. The details of technique of treatment and the photographs and illustrations, both of treatment and segmental nerve supplies, are really good, and make the book well worth a place in the library of everyone studying physical medicine.

Recent Advances in Public Health. By J. L. BURN, M.D., D.Hy., D.P.H. London: J. & A. Churchill Ltd., 1947. Pp. viii and 409. Figures 82. Price 25s.

IT is inevitable that a book reviewing the Public Health progress of the last twenty years should.

be essentially a record of the successes and failures of what might be termed the "Newman era" and its division into three parts concerned respectively with the individual, the community and the environment is both logical and convenient. The sections in the first part on the care of mother and child and on the care of handicapped children are particularly well done. Brief but adequate accounts are given in the second part of such important community developments as the Papworth Tuberculosis Colony and the Peckham Health Centre experiment. In the third part the number of subjects dealt with is small but several of considerable current interest, such as the high-temperature-short-time method of milk pasteurization, are fully covered. The accounts given of many of the subjects are descriptive rather than critical and many workers within the wide field of public health, e.g. epidemiologists and pathologists, may consider that the subjects which specially interest them have not received sufficient attention.

Health Services in England. By G. R. C.

WOFINDEN, M.D., B.S., D.Ph., D.P.A.

Bristol: John Wright & Sons, Ltd., 1947.

Pp. x and 191. Price 10s.

THIS book describes and discusses the health services in England as they were in 1946, and in a postscript deals with the National Health Service Act of 1946. It should prove useful to those who have administrative posts under the new Act, in that it provides a short and readable background against which their current problems should be viewed. Some sections are of general interest and there are but few who would not be intrigued by the work on "problem families" that has been bravely begun at Rotherham by Dr. Wofinden and his colleagues.

NEW EDITIONS

In view of the many changes in social legislation during the past three years considerable revision has been necessary in the preparation of the ninth edition of Jameson and Parkinson's *A Synopsis of Hygiene*, by G. S. Parkinson, C.B.E., D.S.O., M.R.C.S., L.R.C.P., D.P.H. (J. & A. Churchill Ltd., 28s.). The re-planning of the Health Services, new regulations under the Education Act, 1944, new rules with regard to the diploma of public health, the National Health Service Act, and the National Insurance Act, have all been incorporated, and sections on the antibiotics and DDT are among the new material added.

A NEW chapter on the protective mechanisms of the body and a number of photo-micrographs of specimens from human material have

been added to *A Textbook of Histology*, by Evelyn E. Hewer, D.Sc., in its fourth edition (Wm. Heinemann (Medical Books) Ltd., 21s.), which has been revised throughout. Section cutting, methods of staining and formulae of solutions are given in the appendix to the new edition, which is well printed and generously illustrated.

The Anatomy of the Nervous System, by Stephen Walter Ranson, M.D., PH.D., revised by Sam Lillard Clark, PH.D., in its eighth edition (W. B. Saunders Company, 32s. 6d.) has been subjected to some change of arrangement in revision, and new material and illustrations have been added. The last chapter is devoted to a laboratory outline of neuro-anatomy. The work is beautifully produced, both as regards text and illustrations, which number 417. There is a useful bibliography.

THE thirteenth edition of *Hey Groves' Synopsis of Surgery*, revised by Sir Cecil P. G. Wakeley, K.B.E., C.B., D.Sc., F.R.C.S., F.R.S.E., F.A.C.S., F.R.A.C.S. (John Wright & Sons Ltd. 25s.) contains a new chapter on the use of penicillin and the sulphonamide drugs in surgery. Advances in vascular surgery, chest surgery, neuro-surgery, and surgery of the ductless glands have been incorporated. The Editor's concluding remarks to his preface, "that as a student he carried the first edition about with him in the wards and out-patient department", commends this well-known synopsis to all students and practitioners.

O'Meara's Medical Guide for India and the Tropics, by H. W. Williamson, O.B.E., M.D., M.R.C.P., F.R.C.S.ED., Lieut.-Col. I.M.S., in its fifth edition (Butterworth & Co. (Publishers) Ltd., 30s.) contains a number of new articles, and extensive rewriting has been carried out, the result of which is a remarkably complete compendium for the use of those practising in tropical countries.

COMPLETE rewriting of the chapter on endotracheal anaesthesia has been undertaken in the preparation of the fourth edition of *Essentials of General Anaesthesia*, by R. R. Macintosh, M.D., F.R.C.S., D.A., and Freda B. Bannister, M.D., D.A. (Blackwell Scientific Publications Ltd., 30s.), and among other additions is a new chapter on trilene. The illustrations, which total 247, are an attractive feature of the new edition.

Vade Mecum of Medical Treatment, by W. Gordon Sears, M.D., M.R.C.P., in its fifth edition (Edward Arnold & Co., 10s. 6d.) has been brought up to date in all sections and the appendix enlarged to include new information on the sulphonamides and penicillin.

NOTES AND PREPARATIONS

NEW PREPARATIONS

ANALJOL, a methyl aspirin preparation for external use in the treatment of neuritis and rheumatic affections, is supplied in the form of a non-staining, non-greasy liniment, which is stated to be easily absorbed by the skin and to possess a combined analgesic and counter-stimulant action. The manufacturers are Kay-lene Ltd., Waterloo Road, London, N.W.2.

EKAMMON tablets (acid acetylsalicylic 0.33 gm., acid ascorbic 20 mgm., menaphthone 0.33 mgm.) have been prepared, by the inclusion of menaphthone to counteract the prothrombin-reducing action of acetylsalicylic acid, and of ascorbic acid to supplement the accelerated excretion in the urine which may lead to C-avitaminosis, to prevent the ill-effects which often follow prolonged administration of acetylsalicylic acid. Ekammon tablets are supplied in containers of 50, 100, 500 and 1000 by Ward, Blenkinsop & Co., Ltd., 6 Henrietta Place, London, W.1.

GELUSIL, a new antacid adsorbent supplied in tablet form, each tablet containing magnesium trisilicate 7.5 grains (0.5 gm.) and dried aluminium hydroxide gel 4 grains (0.25 gm.), has been prepared for use in the treatment of gastric acidity and peptic ulcer, and may be taken in combination with other medication, such as phenobarbitone and belladonna. The manufacturers are William R. Warner & Co., Ltd., Power Road, London, W.4, by whom Gelusil is issued in boxes of 50 tablets, price 3s. 2½d. (plus 9½d. tax) subject to medical discount.

HUNTERIAN SOCIETY MEDAL

THE Council of the Hunterian Society have decided to revive this award, competition for which is open to all general practitioners. The subject chosen for the next essay is "The Treatment of Obesity in General Practice", and MSS must be received on or before December 31, 1948. The Hon. Secretary to the Society is J. C. Ainsworth-Davis, Esq., F.R.C.S., 48 Wimpole Street, London, W.1, to whom prospective competitors are invited to apply for further information.

THE EMPIRE RHEUMATISM COUNCIL

At the Annual General Meeting of the Empire Rheumatism Council on December 4, 1947, Lord Horder, the Chairman, discussed several points of interest, among which were the adoption of the *Annals of the Rheumatic Diseases* as the official journal of the American Branch of the International League against Rheumatism, the reopening of the Council's laboratory at the Hospital of St. John and St. Elizabeth, and a pilot survey into the incidence and causes of

rheumatism among miners, to be carried out by the Research Department of the University of Manchester (Nuffield Foundation). The post-graduate courses arranged by the Council are another feature of national importance.

PUBLICATIONS

British Empire Cancer Campaign: Twenty-fourth Annual Report, 1947, contains detailed particulars of the work carried out during the year at the different research laboratories and hospitals. Of outstanding interest are the reports on the use of nitrogen mustards in bronchogenic cancer, the results of experiments with radio-active tracer elements, and the record of the results of an investigation of cellular nutrition and carcinogenesis, which has revealed a direct relationship between growth inhibition and the protein content of the diet.

Hearing Aids and Audiometers (Med. Res. Coun. Spec. Rep. Ser. No. 261) is the report of the Committee on Electro-Acoustics. It is of interest to note that the Ministry of Health has made arrangements for large-scale manufacture of hearing aids for issue to patients under the new National Health Service Act (H.M. Stationery Office, 1s. 3d.).

Diagnostic Agents, by T. D. Whittet, Ph.C., D.B.A., is the collection into booklet form of a series of tests that appeared in the *Pharmaceutical Journal* in April and May, 1947. Although primarily compiled for the use of pharmacists studying for the Diploma in Biochemical Analysis, the booklet should prove of great value to the practitioner, who will find therein full particulars of the diagnostic tests for diphtheria, scarlet fever, tuberculosis, allergy, blood sedimentation, renal function, blood sugar, the prostigmin test for pregnancy, and a number of other useful procedures (Pharmaceutical Press, 2s. 6d.).

BURROUGHS WELLCOME & CO.

THE address of the Burroughs Wellcome Home and Overseas Division is now 183-193 Euston Road, London, N.W.1 (Tel. Euston 4477), where practitioners should in future send communications.

BINDING CASES

Binding cases for Volume 102 (July-Dec. 1947), and those for previous volumes, are available in the form of gilt lettering, price 4s. each. The cases are made to hold six copies after the advertisement pages have been removed; they are not self-binding. Alternatively subscribers' copies can be bound at an inclusive charge of 10s. 6d. per volume; this includes the cost of the binding case and return postage.

The contents of the February issue, which will contain a symposium on "The Present Status of Virus Disease", will be found on page LXXIV at the end of the advertisement section.

THE PRACTITIONER

No. 956

FEBRUARY 1948

Volume 160

EDITORIAL

THE PLEBISCITE

The Practitioner has no party allegiance. We hold that the spirit of moderation is essential to the unity of the medical profession. Without unity a comprehensive medical service cannot function. The majority of the profession greatly desire the creation of such a service, and long before politicians showed any interest in it many doctors were eager but unheeded advocates.

The present deadlock between the Minister of Health and the doctors arises therefore not from a difference of principle but of administration. The Minister is thinking, and is bound to think, of his responsibilities to Parliament, the doctors of their patients. The first considers authority, the second freedom; for the essence of a doctor's relation with his patients is in mutual confidence, which is lost if he loses his freedom. He expects frankness, which is the foundation of his diagnosis; he must inspire trust, which is often the prerequisite of all cure, even the cure itself. As we all know, such a relation obtains with difficulty between any full-time servant of the State and the private citizen.

If any British Government should aim, openly or secretly, at a State Service in the totalitarian sense of the word, it would be the public duty of doctors to oppose it. Many do oppose the present scheme because they fear that the basic wage and the refusal of a right to appeal are steps towards such a State regimentation. Is this suspicion justified? It is deep and strong and no agreement is possible until it is removed.

It has been said, "Let us try the plan, and amend it later." But what amendment could restore lost confidence? Faith is a delicate plant as every doctor knows. It is not a commodity to be bought and sold.

The gap therefore between Ministry and doctors, although small in extent, is deep. It is a conflict of responsibilities. Solution lies in agreement that the doctor must be secured in the prestige of independence, that the Minister shall not be required to answer for faults in the service which he has no power to remove. As both are essential to the success of the scheme, and to justice, a solution should not be far off. The difference between the Minister and the British Medical Association can be bridged in an atmosphere of goodwill. The time for amendment is *now*.

VIRUSES AND DISEASE IN MAN

By C. H. ANDREWES, M.D., F.R.C.P., F.R.S.

From the National Institute of Medical Research.

THE word "virus" probably brings two ideas to the mind of the non-specialist. First, he may think of it as something which has upset preconceived ideas of the nature of life by virtue of the fact that it can be crystallized. Secondly, he knows that viruses cause a lot of diseases which are particularly baffling to the medical profession. This article will attempt to bring these two concepts into their proper perspective.

THE PHYSICAL PROPERTIES OF VIRUSES

Size.—Viruses range in size from the approximately 250 m μ (0.25 μ) diameter of psittacosis down to the 10 m μ of the agents of poliomyelitis and foot and mouth disease. Thus the largest are about equal to the size of small bacteria; the smallest to some of the larger protein molecules. Within the 10-250 m μ range they are fairly evenly distributed, with vaccinia, herpes and rabies among the larger ones, influenza near the middle (about 80 m μ) and yellow fever, with some of the encephalitis viruses, down among the midgets. There are no indications of a break in the series such as might suggest that the smaller were of entirely different nature from the larger ones. The sizes of many of the viruses were first determined by filtration through the collodion membranes of graded porosity (gradocol membranes) described by Elford. Later measurements by means of centrifugation, microscopy and other methods have in general confirmed the estimates obtained by filtration.

Shape.—Most viruses affecting animals ("animal viruses", for short) are roughly spherical. Some of the larger ones, such as vaccinia and others of the pox group, seem to be brick-shaped, and within them portions of greater density can be shown in electron micrographs (Rivers, 1943). Quite otherwise is it with many of the viruses which attack bacteria and higher plants. The bacteriophages are now generally agreed to fall into the virus group and are increasingly coming to be called "bacterial viruses". Many, but by no means all, of them are seen in electron micrographs to consist of a head of definite size, shape and structure and a tail of definite length—the whole looking somewhat like a spermatozoon or a tadpole. There is, however, no reason to believe that the tails are organs of locomotion! On the other hand, many of the plant viruses exist in the form of thin rods, of which the length is fairly constant but varies to some extent about a mean. The rods seem to consist of smaller units aligned end to end, but there is uncertainty as to how far the rods can be broken up without inactivating the virus. It is the alignment of these rods in parallel bundles which permits the crystallization of such a virus as that of tobacco mosaic. Such an arrangement

should strictly be called a para-crystal, but there are other, spherical viruses which can be aggregated into true crystals. It is no longer felt by many people that the faculty for orderly arrangement to form a crystal is a valid reason for regarding an agent as non-living.

Electron microscopy.—The shape, the evidence of internal structure and, in the case of bacterial viruses, the existence of tails, have been revealed by the higher resolution which is possible with the electron microscope. New and better pictures of viruses are being published every month. The most striking recent development has been the shadowing technique of Williams and Wyckoff (1945), in which molecules of a suitable metal, usually gold, evaporated in a high vacuum, fall at almost glancing incidence on the virus preparation. The virus bodies are in this way caused to throw a shadow, so that when an electron micrograph is taken the image is one of excellent contrast and relief, giving information as to the three-dimensional features of the virus bodies. The plate (p. 85) shows pictures of vaccinia virus and of a staphylococcus bacteriophage taken with and without "shadowing".

It must be remembered that the electron microscope has two serious limitations. It is possible to examine only dried material in a high vacuum; this means that great precautions are necessary to avoid the production of artefacts in the drying process. Also, one cannot take pathological material from a disease of unknown etiology and "look at it under the electron microscope to see if there is a virus there". Before virus material is worth examining it must be propagated in a suitable host until it can be obtained in large quantity and then submitted to a greater or lesser amount of purification so that a given material may consist more of virus than of miscellaneous debris.

Chemical composition.—So far as is known all viruses contain nucleoprotein. Some of the smallest, most simple ones seem to consist entirely of nucleoprotein, but the majority of animal viruses are more complex. Vaccinia, for instance, is thought to contain also lipid material, copper and flavin and, in its surface structure, at least three or four different antigens (Rivers, 1943). It seems that such a virus is not much more simple than bacteria. Nevertheless there has been great difficulty in showing with any virus that purified preparations have enzymatic activity of their own; enzymes from host cells seem rather easily adsorbed on the virus surface. Recently it has been claimed (Knight, 1946) that influenza virus propagated in mice contains mouse protein as an integral part of its make-up, and that when the same virus is grown in fertile eggs, then egg protein instead enters into its composition. Others, however, are not convinced that the results obtained cannot be explained by imperfect purification of the virus. The tobacco mosaic virus can be obtained free from all host protein: possibly it is easier to purify.

From tissues infected with some of the larger viruses, antigens, sometimes called soluble antigens, can be obtained; these antigens are smaller than the

viruses themselves and are probably derived in most instances by the breaking off of something from the virus surface. They are recognized by *in vitro* serological tests, such as precipitation and complement fixation, and are known for vaccinia, influenza, lymphocytic choriomeningitis and some other viruses.

VARIATION AMONG VIRUSES

To the laboratory worker in this field the variability of viruses is one of their most important characters. If, for instance, he is trying to infect a laboratory animal with a virus from a human disease, he tries to adapt it to a strange host; this in fact amounts to selecting variants which can grow in the new environment. Variants of viruses may, in many instances, be equivalent to mutations of higher organisms; they may affect the affinity of the virus for the tissues of various hosts, the virulence of its attack on cells of one particular host, resistance to external influences, and antigenic structure. Some virus-mutants have proved a veritable godsend: such is the 17D strain of yellow fever virus which has permitted the safe vaccination of millions of people. Vaccinia virus, too, is probably a mutant of variola.

NATURE AND ORIGIN OF VIRUSES

The facts so far described give some basis for discussion of what viruses are. In many respects they quite obviously act like living things: the facts of variability combined with self-replication make them automatically subject to the forces of natural selection. Few, if any, epidemiologists will deny that most virus infections behave like other infections: the success of quarantine in keeping rabies out of Britain and foot and mouth disease out of Australia shows that these viruses do not readily arise *de novo*. There is only one matter of dispute: some think they are highly specialized parasites, degraded, as so many parasites are, from the more complex make-up of larger ancestors; others, that they have been, or are still being, derived from some part of the host cell which has broken away from its environment, having the ambition to set up on its own as an independent organism. The arguments in favour of the latter view are most cogent in the case of the plant viruses. Among these are the ones which have been crystallized; all that have been studied seem to be in the lower size-range and all may consist only of nucleoprotein. Further, a case can be made out for *de novo* origin rather more convincingly than for any animal virus. The nature of the plant viruses may be said to be an entirely open question. As to the bacterial viruses, it is hardly possible to look at such a tadpole-like object and believe it to be anything but an organism. Burnet (1945) has suggested that "phages" may be the only survivors of a pre-cellular form of living thing.

Whatever be the verdict on plant viruses, nearly all workers on animal viruses conceive of them as organisms in which specialized parasitism, simplification of structure and diminution in size have gone hand in hand.



FIG 1 —Staphylococcal phage gold shadowed $\times 30,000$



FIG 2 —Vaccinia virus gold shadowed $\times 20,000$



FIG 3 —Staphylococcal phage $\times 30,000$



FIG. 4 —Vaccinia virus $\times 35,000$

The larger ones are admittedly organisms and, running down the scale to the foot and mouth virus, there seems singularly little evidence for an essential change in properties.

WEAPONS OF ATTACK

Viruses are, so far as is known, all intracellular parasites; the disease-producing ones probably act chiefly by multiplying within cells, in due course destroying the cells and correspondingly damaging the host as a whole. In many instances, inclusion bodies, consisting of cytoplasmic colonies of virus, can be found in cells, and these are often of diagnostic value (e.g. molluscum contagiosum). Other similar appearances, some in the cytoplasm, some in nuclei, are equally characteristic but are less certainly colonies of virus; intranuclear inclusions may represent degenerative changes secondary to virus multiplication (herpes simplex, varicella).

Many viruses at first cause cells to proliferate excessively and only later to necrose. The proliferation may be relatively slight and necrosis will then dominate the picture. If, however, the virus is less damaging, proliferation alone may for months represent the only reaction of the host (infective warts). It is this known capacity of a virus to induce cell multiplication over a long term which is one of the potent arguments in favour of the virus theory of cancer.

Besides these direct effects of viruses multiplying within cells, there have recently been revealed so-called "toxic" effects of viruses, apart from any virus multiplication. This was first shown during the war for rickettsiæ, the group of organisms which cause typhus and related fevers and which seem to stand between the viruses and the bacteria. Very large doses of rickettsiæ given to mice intravenously will kill them within twenty-four hours and without apparently multiplying. Only the living bodies of the organisms, not any products thereof, were effective; it is thus doubtfully justifiable to talk of a toxic action. Similarly, very large doses of influenza virus will, in the absence of multiplication, rapidly produce certain pathological changes: they can cause keratitis when injected into the anterior chamber of a rabbit's eye, encephalitis when put into a mouse's brain, or pneumonia in its lungs (Henle and Henle, 1944). These findings may help to explain why influenza, of which the virus can only multiply in the respiratory tract, can cause headache, backache and pains in the limbs.

Fresh light has recently been thrown on the means whereby a virus introduces itself to a susceptible cell. Hirst (1942) discovered that influenza viruses had the property of agglutinating the red cells of fowls and some mammals. This has turned out to be due to specific adsorption on to the red cells. This adsorption is not permanent, for after some hours the virus becomes spontaneously eluted, taking with it as it comes off something from the red cell's surface. Burnet and his colleagues (1947) have produced evidence that the virus can react with the ABO-group-active substances on

the cell's surface. Hirst (1943) carried out experiments with ferrets, the results of which indicated that the virus-red-cell reaction might afford a clue to the reaction between the virus and cells of the susceptible respiratory tracts.

Variation among viruses has already been mentioned. It may be that this property should be included among the viruses' weapons of attack. Many different serological races occur within the two big groups, A and B, of influenza virus. The possibility must be considered that, as a human population acquires a resistance to current strains of virus, a mutant strain of "flu" virus occurs, sufficiently different to be able to infect a herd which is priding itself on its immunity. A chance mutation, diverging particularly widely from type, may have set in motion the pandemic of 1918-19.

PATTERNS OF DISEASE PRODUCED BY VIRUSES

Childhood infections.—The diseases often thought of as typical virus infections are measles, rubella, chicken-pox and mumps. There is apparently little or no natural immunity to these once passive maternal immunity has waned, so that contact with a small number of virus particles can infect. Such contact usually occurs in childhood, and the illnesses in question are therefore mainly children's diseases. So too, in the old days, was smallpox. Immunity following these infections is commonly lifelong. If there is no contact with virus during childhood, severe epidemics in adults may result; the serious results which followed the first introduction of measles into the Fiji and Farøe Islands are well known. Yellow fever has been mainly a childhood disease in West African natives but, for obvious reasons, a disease of adults in Europeans.

Recurrent infections.—Some viruses, unlike those in the first group, seem to leave behind no permanent immunity. Pre-eminent among these are colds and influenza. Now that two antigenically unrelated influenza viruses, A and B, are recognized it is not surprising that two attacks of influenza can occur within a short time. Indeed on a few occasions virus A has been recovered from a patient in one such attack, B from the other. As already mentioned, serological variations within each virus-group further confuse the picture. Nevertheless, it seems certain that the common viruses affecting the upper respiratory tract do not produce solid immunity. Possibly their access to the exposed surfaces of cells permits them to invade even in the presence of a humoral immunity.

Conditioned infections.—The experience of those working with the common cold virus shows that instillation of known active virus into the noses of human volunteers infects only 40 or 50 per cent., although many of those who resist are at other times subject to colds. It is commonly believed that exposure to draughts and other such incidents determine the onset of a cold. Clearly, then, mere contact of virus and host are not enough to

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produce overt infection. Most of us are probably exposed to the poliomyelitis virus, yet few develop recognizable infection and still fewer show paralysis. Unknown factors determine whether or not a simple infection goes on to serious involvement of the central nervous system.

Infections acquired from other animal species.—Many of the more recently recognized virus diseases belong in this category. Psittacosis, acquired from contact with parrots, is a well-known example. Most animal-to-man infections seem to be little if at all infective from the first infected subject to other human beings; but there is evidence that with psittacosis and related viruses short man-to-man chains of infection occur. Several types of insect-borne encephalitis have been recognized in recent years: such are the Eastern, Western and Venezuelan types of equine encephalomyelitis and St. Louis encephalitis of the New World, and the Japanese B encephalitis of the Far East. These are mosquito-borne; man and the horse seem alike to be infected accidentally, the natural host of all or most of these viruses being probably in birds. Recent evidence suggests that the normal cycle of the virus may be from bird-to-mite-to-bird; that in the summer only, the mosquito acts as an additional vector and then man and the horse may suffer. Lymphocytic choriomeningitis, from wild mice, and feline pneumonitis are examples of animal diseases spreading to man by the respiratory route. Yellow fever is an example of a disease which apparently may be truly a human infection with a cycle man-to-Aedes-mosquito-to-man; but which is, at least in South America, fundamentally an animal disease, jungle yellow fever, with a cycle monkey-to-hæmagogus-mosquito-to-monkey. The Aedes-man cycle has become superimposed on the other, probably within historical times. Burnet (1945) has advanced the view that this sort of thing has been constantly happening. Most virus infections are probably normally subclinical, the result of age-long association between host and parasite. We are only conscious of the existence of virus infections when the equilibrium is imperfect. Burnet suggests that most of the obvious virus diseases of man are of relatively recent origin, having been originally caught from some animal; they have so far adapted themselves that they will now spread from man to man and are thus now human diseases, though newcomers. In the course of years or centuries host-virus equilibrium will be established and the symptoms of infection will sink below the clinical level.

"Spontaneous" virus diseases.—Whether or not such interesting speculations reveal the truth, what is quite certain is that many virus infections are commonly latent. Herpes simplex probably infects human beings first as a stomatitis in infancy; thereafter many people apparently never get rid of it completely. It relapses into obscurity for months or years, only to blossom out in the form of fever blisters with the onset of a cold, fever or other stimulus. Often the same site around the nose or lips is involved in each attack. The general view is that the virus is present in the tissues all the time,

some stimulus such as a cold being necessary to upset the host-virus equilibrium; but to the casual observer each attack of herpes comes from nowhere. So-called homologous serum jaundice is produced by injecting blood, serum or plasma from normal people into other normal people, especially when large serum pools are used. The agent certainly seems to be a virus; this was at first thought to be identical with the virus of infective jaundice but is now believed to be different. Spontaneous jaundice due to this virus has not yet been recognized; it must commonly be entirely latent.

Laboratory workers deliberately transferring tissues from one animal to another repeatedly uncover by such means latent viruses of which the existence was unsuspected. With this knowledge it can be seen how easily a particular manipulation might appear to cause a new virus to appear. To those who believe in the virus theory of cancer, this is the example, *par excellence*, of a latent virus infection, of which the open manifestation is conditioned by many complex factors.

A new line of approach to the problem of protection against viruses is opened up by rapidly expanding knowledge of the "interference phenomenon" in virus diseases. The existence of one virus in the host seems sometimes to preclude attack by a second virus; the two viruses in question need not be antigenically related. Such interference has been demonstrated in the living host, in infected chick embryos and in tissue cultures. Parallel results are described among the bacterial viruses, when the virus first gaining access seems either to alter the surface of the bacterial cell or to pre-occupy a key enzyme system, so that a later-coming virus knocks vainly for admission. The first virus, even when inactivated by ultra-violet light, may be able to block the entrance of the second (Delbrück and Luria, 1942). Experiments in fertile eggs infected with influenza and other viruses give similar results (Henle and Henle, 1944, 1945), and the same may be shown in the infected mammalian host (Andrewes and Elford, 1947). It does not need much imagination to conceive of all sorts of possible developments from study along such lines.

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MODE OF TRANSMISSION OF VIRUS DISEASE

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THE transmission of any infectious disease is a complex mechanism consisting of a number of integrated parts and stages:—(1) The source of the infection; (2) the manner in which the infective agent leaves the body of the first host; (3) the method of transfer to the new host; and (4) the route by which invasion of the new host occurs. Man is the source of most of his own bacterial diseases, but many virus infections of man may be derived directly from animals or birds, e.g. cowpox, lymphocytic choriomeningitis, psittacosis, rabies, or indirectly by insect bite as in the various encephalitides, Rift Valley fever and yellow fever.

As in bacterial infections, evidence of the convalescent carrier state is found in some of the virus diseases. In psittacosis, there is evidence in both animals and man that the virus may be harboured for long periods after apparent clinical recovery. Convalescent carriers are known to be unusual in poliomyelitis, but the virus has been isolated from the faeces of a patient on the 123rd day after onset, and also from a very small number of pools of tonsils and faeces from children in an inter-epidemic period in California. These latter may be either subclinical cases or carriers. Similarly, in the common cold and influenza, there are probably healthy carriers between epidemic periods, although present laboratory methods are not sufficiently sensitive to permit their identification. Herpes simplex is another good example, and it is possible that convalescent carriers also occur in other virus diseases, such as virus hepatitis and the types of gastro-enteritis attributed to virus infections.

The route or vehicle by which the virus may leave the first host will depend largely upon the site of the lesion, e.g., the skin in variola; lachrymal discharges in trachoma; the nasopharynx and oropharynx in influenza, measles, variola; the faeces in psittacosis in birds, infective hepatitis and poliomyelitis; the urine in lymphocytic choriomeningitis; the genital tract in lymphogranuloma venereum; the blood stream *via* insect vectors in yellow fever; the placenta in variola; and by direct injection of blood, e.g. virus hepatitis. All these examples have their counterpart in bacterial or protozoal diseases. These examples are, for the most part, unquestioned, being based upon virus isolation, epidemiological studies, and the results of methods used to control the disease. Of course in some of these instances the virus has been isolated from certain sites in the body where there is no apparent lesion, e.g. nasopharynx, oropharynx and intestinal canal in poliomyelitis, and where the significance of the finding is not entirely understood. In

other instances, it is possible that methods of study and virus isolation have not been sufficiently sensitive or applied at the correct period in the infection to detect a possible source, e.g., the naso- or oro-pharynx is a suspected but unproven site in infective hepatitis.

It is when the method of transfer to the new host and the route of invasion in the new host are discussed that most of the uncertainties creep in, as a result of ideas or theories which cannot be quite turned into definite conclusions or facts, chiefly because of inefficient or non-existent tools. The methods of transfer from one host to another are (1) direct contact; (2) droplet and air-borne; (3) food-borne; (4) injection: (a) insect bite, (b) mammalian bite, (c) syringe; (5) transplacental. In the following list are set out the possible modes of transmission of the virus diseases affecting man, with the viruses arranged in their generally accepted groups. In the case of many virus diseases, only a single mode of transmission is recognized, other than laboratory infection, e.g. mosquito bite in yellow fever; in others, such as variola, there are several alternatives, and in yet others, several possible routes none of which is proven, e.g. poliomyelitis.

Direct contact.—Between skin or mucous surfaces: lymphogranuloma venereum, rabies, warts.

Droplet.—(a) Droplet or air-borne from the upper respiratory tract: chickenpox, common cold, ? gastro-enteritis of infants and adults, glandular fever, ? infective hepatitis, influenza, measles, mumps, ? poliomyelitis, psittacosis, rubella, smallpox, ? zoster.

(b) Fomites—contaminated by droplets or contact—the above diseases, and in addition, herpes simplex, inclusion blennorrhœa, lymphocytic choriomeningitis, trachoma.

Food-borne (milk-borne, and so on).—? gastro-enteritis of infants and adults, infective hepatitis, ? poliomyelitis.

Injection.—(a) Insect bite: dengue, equine encephalomyelitis, Japanese *B. encephalitis*, St. Louis encephalitis, Rift Valley fever, Russian spring-summer encephalitis, sandfly fever, yellow fever. (b) Mammalian bite—rabies. (c) Syringe: infective hepatitis, homologous serum hepatitis.

Transplacental.—Infective hepatitis, rubella, varicella, variola.

In the group of diseases in which the virus is probably transmitted from case to case in droplets expelled from the upper respiratory tract there are localized and generalized infections. In the common cold and influenza the infection appears to be localized chiefly in the superficial cells of the upper respiratory tract and the bronchiolar epithelium, and may be widely disseminated by sneezing and coughing. The larger droplets produced in this way have been shown to travel 2 to 3 feet, or perhaps a little more, before they fall to the floor. The smaller droplets remain in suspension for several minutes, and about half of the droplets from a sneeze are said to be still in suspension at the end of half an hour. These droplets may or may not contain one or more of the organisms in a small quantity of secretion or water. As the moisture evaporates, the nuclei are left suspended. It has been suggested that the term *droplet infection* should be restricted to direct conveyance of droplets to an individual within 3 to 4 feet of the primary

host. The less intimate transfer by droplet nuclei or small dust particles suspended in air beyond this distance may be classed as *air-borne*.

A very large part of the new concept has been based on artificial dissemination of organisms into the air. Because of the technical difficulties little work has been done in relation to the detection of living virus in the air, and the rôle of this mode of spread has been examined largely by indirect methods, such as irradiation of the air with ultra-violet light in schools. Infected particles of dust may also pollute the air. These particles will have been the nuclei of heavier droplets, or gross discharges from the nose, throat, gastro-intestinal and urinary tracts, which have dried upon reaching the bed-clothes, floor, or clothes, and are redispersed into the air when the dust is disturbed. Here again, the heavier particles, if not inhaled, will fall rapidly and only a small number of lighter, smaller particles may remain suspended in the air to be inhaled.

It is only quite recently that the possibility of infection by *ingestion* of virus-infected material has been seriously considered. We now have evidence that the viruses of poliomyelitis and infective hepatitis may infect by this route, and in some circumstances the intestinal-oral route may be the main route of transmission of these diseases. Certain types of gastro-enteritis of infants and adults, attributed to a virus, may also result from ingestion of the virus, although evidence on this point is lacking.

The modes of transmission are also closely linked with the virus requirement of living cells for growth, and the stages of the life history of the virus. The usual sequence of events is: (1) transmission to the new host; (2) entry into the new host (3) spread through the tissues of the host; (4) localization in selected cells; (5) action on parasitized cells [(i) necrosis, (ii) hyperplasia {necrosis or (iii) symbiosis}; (6) excretion from the host, direct or indirect transfer to a new host.

Some of the viruses will now be considered individually in the various groups. At the present moment there are no specific means of control of a number of virus infections and further progress rests partly on increased knowledge regarding the mode of transmission. When the diseases in which the virus may be transferred from one host to another, by direct contact or droplet infection, are considered, and the possible routes of entry in these diseases, it must be admitted that in practically none of them is there unequivocal evidence of the real importance of any particular path.

LYMPHOGRANULOMA VENEREUM

There can be little argument that the virus is usually transmitted from case to case by direct contact at intercourse. The clinical course in the male is more often diagnosed and amenable to treatment than in the female, in whom small chronic lesions on the labia, unaccompanied by involvement of superficial lymph glands, may remain unrecognized, and such individuals act as a source of infection in a state approaching a "carrier" for a considerable period.

THE COMMON COLD

A virus is generally considered to play a large part in this disease but, because of the lack of a suitable small susceptible experimental animal, knowledge of the exact mode of transmission and the factors influencing its spread are limited. Recourse has recently been made to the use of human volunteers in large-scale experiments in this country, and it is hoped that the work of the Medical Research Council team will throw some light on these questions. It has usually been assumed that the infection is spread by droplets expelled from the nose or mouth into the air, and inhaled directly or as *air-borne* particles, so that it is of considerable interest to see this conception being questioned in a recent editorial on air-borne infection. "It is, of course, not yet by any means certain that aerial transmission is the only or even the most important factor in the spread of the common cold" (*Brit. med. J.*, 1947). I would certainly agree that it is possible that the dirty handkerchief and fomites may play a large part in the spread of this disease.

INFLUENZA

In epidemic periods, or winter time in any year, it is presumed that the influenza viruses are spread by droplets, but at other times it is possible that spread is maintained by fomites. Andrewes has suggested that in the first place the spread may be a result of the seasonal coughs and colds, without the actual production of clinical "influenza", but the virulence of the virus increases with passage until it causes symptoms and can be spread on its own. Although the majority of cases probably result from direct *droplet* infection, *air-borne* infection may also occur, especially with influenza A virus. The A virus, in the form of infected animal or egg tissues, has been found to survive a week at room temperature when dried on a blanket or in dust, and at least forty minutes when dried on glass, but only ten minutes when dried on the hand. The B virus is by contrast very labile, being rapidly inactivated when dried either on the palmar surface of the hand, glass, or rubber sheeting.

One of the most interesting questions which is linked to all the factors concerned in transmission of influenza, is the whereabouts of the virus between epidemics. The virus has, in a few instances, been recovered from garglings of healthy persons during epidemics, but there has been no good evidence of recovery of virus from carriers during the usual period of about twenty months between epidemics of virus A influenza. Our present methods are probably not sensitive enough to detect small amounts of virus present. Burnet (1945) has suggested that perhaps in one person in 10,000 a few virus particles remain latent until such time as suitable conditions for transfer and multiplication arise. The possibility must also be considered that, as Shope (1941) has suggested for swine influenza, an intermediate host may be responsible for interepidemic survival of the virus. At present there is no evidence in support of this theory.

SMALLPOX

This disease is considered to be primarily an infection of the upper respiratory tract and the main mode of spread is by droplet spray or droplet nuclei in the early stages of the disease. Following invasion of the blood stream, macules and papules may appear on the buccal mucosa, but there is some doubt whether or not virus is disseminated from this site at this time. There is no laboratory evidence to support this view, and I have recently failed to grow the virus from extracts of throat swabs from two patients in the stage of papular rash, and one who was in the crusting stage. Rossi (1947) has recently reported the isolation of virus of alastrim from the throat in the pre-eruptive stage and first few days of rash. The virus is comparatively stable, even in the form of moist droplets, but is probably most stable when the disease has reached the crusting stage. Virus inside dry crusts may remain viable for many months in atmospheric conditions, and Downie (1947) has recently isolated the virus from the dust on the ward floor near a bed in which a child was convalescing from smallpox. The patient is infective at least up to the time of the last crust, and virus is probably present on the skin after this stage if untreated, as by frequent baths.

Recent laboratory experience has confirmed the established concept of mild unrecognized cases acting as a source of infection: we have isolated virus from apparently well contacts who had only one or two minute lesions. The virus has also survived in smears and diluted vesicle fluid dried on glass slides for five to six weeks, and from one sample of crusts kept in a glass bottle at room temperature for over a year. One of the most remarkable events in smallpox has been the occurrence of the disease in individuals in whom possible contact was quite untraceable, and the above findings indicate how such infection might take place.

MEASLES

The measles virus has been shown to be present in the nasopharynx and the blood in the early stages of the disease. The nasopharyngeal secretions are considered to be infective early in the disease in the catarrhal or pre-eruptive stage, when the coryza and cough which are present may help to disseminate the infective droplets. The virus has been grown in the developing chick embryo, but without distinctive lesions, and otherwise has only been known to infect primates. Thus, the amount of laboratory work done has been limited, and data for the exact periods of infectivity are not available. Following inhalation, the virus may pass into the blood stream from either the naso- or oro-pharynx, or else the lung parenchyma. The pneumonia which occurs in measles is usually considered to be a virus pneumonia, followed by a secondary bacterial pneumonia, but whether invasion and infection of the lung parenchyma precede or succeed blood-stream invasion is unknown.

CHICKENPOX

This disease is usually considered to be primarily an infection of the upper

respiratory tract, followed by invasion of the blood stream and generalized infection. Fatal cases have shown typical pocks on internal organs, and the disease has been transmitted to the foetus *in utero*. The virus is thought to be conveyed ordinarily by droplet spray, particularly in the prodromal stages, and possibly at the end of the incubation period. Various investigators have found that the careful isolation procedures which were successful in preventing cross-infection in diphtheria and scarlet fever in an open ward did not prevent a few cross-infections of measles and chickenpox. Winslow and others have attributed this difference to the fact that the smaller and lighter viruses could be carried by air currents to a greater distance than the larger and heavier bacteria. This difference may be due to other characteristics of the viruses which aid in their resistance to inactivation and favour spread by fomites. In support of the theory of air-borne spread, Wells in the United States reported that there were fewer cases of chickenpox in classes where the air had been irradiated with ultra-violet light. The conveyance of infection by contaminated hands, clothing, and utensils is probably also an important mode of spread. The crusts of the dried lesions have been regarded as potentially infective, but there is no susceptible experimental animal on which to confirm the truth of this hypothesis, and many individuals with experience in this field do not believe chickenpox is infective after the vesicle stage.

Although immunity is more or less permanent, suggesting a high content of antibody in the serum, serum prophylaxis, even with gamma globulin from convalescent serum, has been unsuccessful.

ZOSTER

There are two clinical types of zoster, referred to as primary or secondary. The clinical and pathological pictures are the same and presumably the etiological agent is the same. Some cases of zoster arise in contacts of either zoster or varicella, and in these cases the infection has presumably been spread by direct contact, droplets, or fomites. However, in the majority of cases the illness appears to have arisen spontaneously or secondary to some exciting factor, such as the injection of arsenic. This suggests that the virus may be carried as a latent infection in the skin, respiratory passages, or elsewhere in the body, until stimulated by some secondary factor, or that carriers spread the infection without ever showing illness themselves. It is generally accepted that the virus causing the clinical entity which goes under this name is closely related to that causing chickenpox, and Harries and Mitman (1947) go so far as to say: "Invasion of the posterior root ganglia giving rise to an attack of *herpes zoster* may be the sole clinical manifestation of an attack of chickenpox".

Neither of these diseases has been transmitted to experimental animals or the developing chick embryo, but virus particles have been seen in stained vesicle fluid and positive complement-fixation and agglutination tests have been performed with such vesicle fluid as antigen and convalescent sera. These tests have shown a cross-immunity between the two viruses. Findlay (1939) has suggested that the viruses are

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secretions are infective. Unfortunately, most of the 40 volunteers used in England in the tests on these secretions were over thirty years of age, so that they may have been immune to the disease. The small number of experiments performed elsewhere were also negative.

In several explosive outbreaks, drinking water contaminated with infected faeces has been incriminated. Thus, although such explosive outbreaks are the exception rather than the rule, and probably infection by either route occurs, the onus appears to rest on the supporters of infected nasopharyngeal droplet spread to prove their case. This disease may also be transmitted by transfusion with infected blood from non-suspected cases, or by accidental inoculation with material in contaminated syringes in clinics carrying out multiple injections and bleedings without adequate sterilization.

ACUTE ANTERIOR POLIOMYELITIS

So much has been written in recent years from the United States and Australia, and in the past year from England, about the mode of transmission of this disease that only the salient points will be discussed here. As in virus hepatitis, there are two possibilities, but in poliomyelitis it has been possible to collect slightly more information because there is a susceptible experimental animal. Here again, as in infective hepatitis, it has been found much easier to isolate the virus from the faeces than from the secretions of the upper respiratory tract. This difference may be due to the stage of the disease at which the specimens have been collected, or to differences in quantities and qualities of these specimens and the virus which they contain. Thus, when comparing the relative importance of droplet inhalation and the intestinal-oral routes, too much stress should not be placed on the ease and frequency of virus isolation from faeces.

The virus can be isolated from the faeces of practically every obvious case, most abortive cases, and many close contacts, showing no symptoms whatever. By contrast, the virus has, on the whole, been isolated from the nasopharynx comparatively rarely, except in two recent experiments in Baltimore and New York when the virus was isolated from the nasopharynx of nearly half of two groups of cases during the first three days of illness, but not thereafter. It is possible that more of them may have had virus in this site before the onset of symptoms. The virus was found also in the throats of 2 of 28 healthy children in a playground where a case had played. The serum of these children had antibody against the homologous virus when tested one year later.

The virus has been isolated from flies trapped in the region of cases, and from food contaminated by infected flies. In these cases it was believed that the flies merely conveyed the virus on their feet, but recent work by Melnick and Penner (1947) suggests that virus multiplication may occur in certain flies. The virus has also been found in sewage from areas where cases are occurring. The virus is remarkably stable in water and sewage. It is said to have survived three months in water at room temperature.

closely related or identical, the condition of the host determining the resulting disease.

It is suggested that zoster occurs when the ordinary virus of chickenpox gains entrance to the nervous system of a patient whose other tissues possess either partial or complete immunity.

RUBELLA

This is usually a mild disease of moderate infectivity, presumably spread by droplet infection. Recently, however, it has come into great prominence by the observation that the *fœtus*, especially in the early months of pregnancy, is susceptible to infection with this virus, which may cause severe and persistent damage, resulting in malformation at birth. The more common abnormalities are malformation of the heart, mental deficiency, deaf mutism and cataracts. It has been suggested by Australian workers in this field that certain strains may be much more virulent than others, but the question whether the suggested higher incidence in Australia was due only to more intensive search for the condition has yet to be determined. It is interesting to note that second attacks are said to occur more often than in measles. It is obvious that in order to clarify the position more careful observations must be made in cases of infection with other virus diseases in pregnancy. When a pregnant mother is exposed to rubella for the first time, in the early months of pregnancy it is advisable to inject her with convalescent rubella serum or gamma globulin from pooled adult serum, in order to try and prevent infection.

INFECTIVE HEPATITIS

(Infectious hepatitis, hepatitis virus A infection)

From the viewpoint of most epidemiologists, this disease was considered in the past to be transmitted by infected droplets from the upper respiratory passages.

When the disease was associated with dysentery in many cases in the Middle East in the 1914-18 war, the possibility of alimentary infection was raised. However, careful field studies by Booth and Okell (1927-28), Pickles (1939) and others in this country since 1928, have supported the conception of a droplet infection from the upper respiratory passages. During the second world war the disease was once more epidemic in the Middle East, as elsewhere, and the conditions under which it arose once again stimulated observers on the spot to favour ingestion of contaminated excreta as the most likely method of spread, although this mode of spread did not seem to apply to the disease usually seen in temperate climates.

No susceptible experimental animal is available, so that the only way further evidence on these points could be gained was the inoculation of human volunteers.

In these experiments, hepatitis was produced by the oral administration of *fæces* collected from patients several days before to several days after the onset of jaundice. No evidence was obtained that virus was present in the nasopharyngeal or oropharyngeal secretions from the onset of symptoms to after the appearance of jaundice. Tests for the presence of virus were not made in these cases before the onset of symptoms. It is possible that it is at this time that the naso-/oro-pharyngeal

may take place by fomites or air-borne infection. Transmission in man is presumably by means of air-borne infected droplets, since this is a systemic disease known to involve the lung in man, and the virus has been isolated from the nasopharynx. The prevalence of disease caused by this particular virus is being investigated in this country, but whether this or some other unidentified virus is responsible, a large percentage of the group of infections producing the syndrome of non-bacterial benign lymphocytic meningitis is probably spread by droplets.

HERPES SIMPLEX

This is one of the most interesting of the virus diseases because of the fact that once a patient has become infected he appears to harbour the virus for life. Neutralizing antibodies for the virus appear soon after the onset of infection and also persist, but appear unable to keep the virus in check. There is no evidence that infection is ever eliminated. The virus is quite widely spread throughout the community, but infection is probably related to density of population. Thus, Burnet (1945), in Melbourne, found that the incidence was much higher in public hospital patients (93 per cent. in both adults and children) than in university graduates (37 per cent.). The virus has recently been shown to be responsible for many cases of aphthous stomatitis in infants. It may be carried in the saliva by infected individuals, but the manner in which the cases occur indicates that spread is not by air-borne infection but rather by infected saliva on hand, handkerchief and utensils. In spite of the ease with which saliva can be contaminated, and the opportunities for widespread infection, especially in winter, the low figure in the university graduates indicates that transfer of infection after infancy is relatively difficult.

MUMPS

This is a disease of low contagiousness, and in uncomplicated cases there are no respiratory symptoms. It is suggested that spread by droplets in such cases is unlikely. Epidemics of mumps unaccompanied by upper respiratory tract infection are not explosive and rapid, but tend to be prolonged. These facts suggest that mumps should not be regarded as a true air-borne disease but rather as one in which droplets of saliva and articles contaminated by them play the largest part in transmission of the disease. It is now usually accepted that mumps is a generalized disease. For this reason it is interesting to note that, in contrast to measles, immune gamma globulin does not appear to have been very successful in the prophylaxis of this disease.

RABIES

The occurrence of two cases in London last year in soldiers bitten abroad awakened interest in possible modes of transmission and the possibility of infecting contacts. The vast majority of cases occur, of course, following the bite of a rabid dog or other animal. In certain cases, however, the animal may not actually bite, but only scratch or claw the skin. In all such cases rabies may follow, but only rarely. The virus is said to have passed through unbroken skin, but this must be a great rarity. There have also been cases

It would appear that first the virus may be present in, and disseminated from, the upper respiratory passages early in the onset of the disease, even before the first rise in temperature, and later is present in the faeces and available for passage by man to man; fly-to-food (milk and the like)-to-man; or by water (no proven outbreak of water-borne poliomyelitis has been recorded). It is obvious that the latter method will be facilitated in tropical regions if sanitary arrangements are inadequate and the right type of fly is present. An examination of the occurrence of obvious cases in England during the recent epidemic has given no clue, as yet, to possible modes of spread. The disease has occurred in every county and the weight of the evidence suggests that the virus was lying latent in a great many foci throughout the country. The factors which initiated this, the greatest epidemic ever recorded in Great Britain, are unknown.

GASTRO-ENTERITIS

There is a considerable amount of evidence that numerous outbreaks of gastro-enteritis in infants, children and adults have been caused by a virus. In many instances there has been a complete failure to incriminate any pathogenic bacteria and no virus has been isolated. Recently, however, two different viruses are reported to have been isolated from two slightly different types of the disease in the United States. It has been suggested that in some epidemics the gastro-intestinal symptoms are secondary to involvement of the central nervous system in a systemic disease. It is probable that a number of different agents may be involved.

There is also a certain amount of data to suggest that there are two distinct types of the disease in Great Britain. There appear to be instances when infants only have been involved in maternity units, and this type usually carries with it a high death rate. In other outbreaks the mothers or staff, as well as the infants, suffer from a comparatively mild form of the disease and deaths occur only in very weak infants, such as prematures. Reimann (1945) has described the production of nausea, vomiting and diarrhoea in volunteers who received intranasal injections of Seitz filtrate of throat washings of cases occurring in an epidemic of gastro-enteritis among university students. This, and the fact that many infants who die following an attack of gastro-enteritis have pneumonia or pneumonitis, has favoured the conception of a droplet or air-borne infection. Others believe spread is direct or by the intestinal-oral route, but so far no clear-cut evidence has been produced for either method of transmission. One common factor is that outbreaks tend to arise when there is overcrowding of mothers and infants and shortage of nursing staff.

LYMPHOCYTIC CHORIOMENINGITIS

This is believed to be primarily an infection of mice, and in the first instance man only becomes infected by contact with infected mice.

The virus is present in the nasal secretions and urine of mice, so that infection

IMMUNIZATION AGAINST VIRUS DISEASES

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LONG before the causative organisms of infectious disease had been discovered it was appreciated that individuals who had recovered from certain illnesses were thereafter unlikely to be affected by them. Acceptance of this fact was implicit in the practice of variolation and vaccination against smallpox many years before immunology, as now known, had been established. The Pasteur method of preventive inoculations given to persons bitten by rabid dogs was one of the earliest attempts to apply the newer methods of specific immunization against a virus disease.

Before considering the methods of immunization and their practical application it may be well to refer briefly to certain features of immunity to virus infections. Whereas it is true that attacks of certain diseases, such as mumps and measles, are usually followed by lasting immunity, in other instances, such as the common cold, there is little evidence of increased resistance following recovery from infection, and in epidemic influenza immunity appears to be of relatively short duration. In general, when there is dissemination of the infecting virus by the blood stream as in the first group, the antibody-forming mechanism responds effectively, whereas in the common cold and influenza the infection remains confined to the mucosa of the respiratory tract with the result that there is a less effective immune response. The second point which is pertinent to the subject is that viruses multiply only within tissue cells and, in that situation, they are not susceptible to the action of antibody upon which immunity mainly depends (the same considerations apply to the rickettsial infections to which references are made later). Antibody will therefore be effective only in so far as it can act upon the corresponding virus before it reaches susceptible cells; it is more likely to act successfully against infections which are usually systemic. In diseases such as measles, smallpox and probably mumps it is almost certain that immediately before and concurrently with the onset of clinical symptoms there is dissemination of the virus by the blood stream from the initial site of multiplication, probably in the mucosa of the upper respiratory tract. Methods of prophylactic immunization aim at the development of antibody which will prevent such dissemination.

METHODS OF IMMUNIZATION

In developing methods of specific immunization recourse to animal experiments has in most instances been a necessary preliminary to field trials against human disease.

Although such work has been valuable in lessening the risk inherent in trying out new methods, the prevention of experimental infection in laboratory animals is, unfortunately, not always followed by equally successful results in the field. Never-

in individuals in regions where rabid animals exist in which there has been no known contact with a rabid animal, but it obviously must have occurred. With regard to transmission from man to man, human saliva has been reported to be infective by several workers, and virus has been reported in the urine in one instance. The cerebrospinal fluid does not contain virus.

HOMOLOGOUS SERUM HEPATITIS (Hæmatogenous hepatitis, hepatitis virus B infection)

This disease is discussed here and not with infective hepatitis because it is usually transmitted by injection, whereas infective hepatitis transmission is by droplet inhalation or ingestion. Homologous serum hepatitis is now accepted as a definite entity associated with the injection of an agent present in the blood (whole blood, serum or plasma) of individuals, apparently normal at the time the blood was collected. Although the virus of infective hepatitis (hepatitis virus A) may be responsible for a certain number of these cases following injection, the majority appear to be caused by an agent (hepatitis virus B) or strain of virus which is immunologically distinct from hepatitis virus A. There is, as yet, no means of identifying the agent in an individual's blood and the safest way to prevent the disease in a transfused patient is to use whole blood, serum or plasma from one donor only. This reduces to the minimum the chance of obtaining both an infective blood and a susceptible recipient.

The blood may be infective in very high dilution and the agent is most resistant to heat and chemicals. Cases have been described in which syringes have been contaminated by withdrawal of the infected blood and then have not been adequately sterilized before use for the next patient. This phenomenon has been described in association with arthritis, diabetes, venereal disease and other types of clinic where numerous venepunctures and injections are carried out. It is preferable that a fresh, dry-heat sterilized syringe and needle be used for each patient in such clinics. Otherwise syringes should be boiled for at least ten minutes, but there is no proof that this will inactivate the suspected agent.

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epidemics of that disease has recently been reported by Gellis, Stokes *et al.* (1945), whilst in children similar successful results have been achieved with relatively smaller doses (Havens and Paul, 1945). On the other hand, the prophylactic value of immune serum against *influenza* has not been established, and the injection of gamma globulin during the pre-paralytic stage of *poliomyelitis* fails to prevent the onset of paralysis (Bahlke and Perkins, 1945). It may be noted that in these two diseases the mode of spread of the virus in the body is not such as would lead one to expect a satisfactory response to antibody injected after infection has been contracted.

One possible complication in the use of human sera for passive immunization is the risk of transmitting serum hepatitis. The use of gamma globulin prepared from human sera will obviate this risk and doubtless other methods will be found for ensuring the safety of human sera to be used prophylactically.

ACTIVE IMMUNIZATION

The methods of active immunization which aim at producing a more durable immunity than can be achieved by passive immunization and which require at least a week, usually longer, before they can become effective, have prophylaxis as their object. Whilst active immunization has proved valuable in the control of such diseases as yellow fever and smallpox in man, and of dog distemper and other virus diseases in animals, active immunization against other infections is still in the experimental stage. For the preparation of vaccines, viruses are usually obtained from the tissues of experimentally infected animals, tissue culture or developing chick embryos. In those human virus diseases, such as chickenpox, herpes zoster and the common cold, in which such experimental infections have not been effected, virus vaccines are not yet a practical possibility. In making vaccines the choice of antigen and method of preparation are all-important, and before their use in routine prophylaxis can be contemplated several criteria must be satisfied: whether or not a vaccine will be safe in practice, whether it will produce effective immunity and how long such immunity will last. If a vaccine will satisfy these requirements then the question arises whether the risk to health and to life from the disease under consideration is such as to warrant general prophylactic immunization, or whether the use of the vaccine should be restricted to times of special risk, i.e., in face of an expected epidemic, or to certain age-groups, or to those members of the community exposed to exceptional risk. Obviously no general answer can be given to these questions, which have to be considered in relation to each individual disease.

Types of vaccine.—Various types of vaccines have been used or are under trial. They fall into three general categories: (1) living fully virulent vaccines, (2) living attenuated vaccines, and (3) inactivated or dead vaccines.

The first kind of vaccine has been used in the past and has usually been injected by a route other than that by which infection is naturally acquired in the hope that serious disease would not result. The practice of variolation whereby variola virus was inoculated into the skin was an example of

theless, the evidence from laboratory tests and observations on virus infections of domestic animals have been of the greatest value in indicating the lines along which successful immunological methods have been developed.

Immunization may be considered under the usual headings of passive and active.

Passive immunization involves the injection of serum containing antibodies derived as a rule from human beings who have recovered from the virus infection against which protection is desired, or less frequently from hyperimmunized animals. Immunity conferred by this method will be at its maximum quickly and will disappear completely within a few weeks. Its use will be limited to emergencies, to give temporary protection to persons exposed to known risk of infection. *Active immunization* involves the inoculation of virus, living or dead, with a view to stimulating resistance to infection with the type of virus contained in the vaccine. If successful this procedure is usually followed by the appearance of specific antibodies in the blood of the inoculated person, and resistance, which takes some time to develop, may persist for months or years. Active immunization is therefore the method of choice when more permanent protection is desired against the risk of repeated exposure to infection.

PASSIVE IMMUNIZATION

The convalescent or pooled adult sera commonly used are of relatively low potency. The perfection of methods for the concentration of the antibodies in such sera by the separation of gamma globulin with which the antibodies are associated seems likely to increase the efficiency of passive immunization. As yet, however, gamma globulins are not generally available in this country. Hyperimmune sera prepared in animals have also been tried in a few diseases. Passive immunization has been attempted in the *treatment* of established virus infections but on the whole the results have not been very encouraging. The reason for this may be that by the time infection is clinically manifest, the virus has already infected most of the cells likely to be attacked and is consequently beyond the reach of antibody.

This explanation is supported by a good deal of experimental evidence (Rivers, 1942). In Rocky Mountain spotted fever, however, Topping (1943) records that hyperimmune rabbit sera given to 52 cases in the first few days of the disease seemed to have a markedly beneficial effect; this finding supports the view that in rickettsial diseases cell-to-cell spread of the infective agent may continue after the onset of illness (Eaton, 1946).

In the *prophylaxis* of virus infections passive immunization has achieved more favourable results. Here the procedure is valuable when susceptible persons have been exposed at a known period of time to a high risk of infection with a virus which is spread by the blood stream, and when the antibody can be administered early in the incubation period. The method has been particularly successful in preventing or attenuating attacks of *measles* in young or debilitated children and is now in general use for this purpose. The parenteral administration of convalescent serum or gamma globulin during the incubation period in *mumps* contacts or at the onset of illness is said to lessen the incidence of orchitis (Leineberg, 1945; Gellis, McGuinness and Peters, 1945). The prevention of infectious *hepatitis* by injection of gamma globulin in 10 c.cm. doses to adults exposed during

viruses in tissue culture and developing chick embryos, together with better techniques for purifying and concentrating the viruses so obtained, seems likely to overcome this disadvantage. Rickettsial vaccines prepared by these methods were used during the recent war against typhus fever; similar influenza virus vaccines have been on trial for several years and inactivated vaccines of other viruses are under investigation. The practice of reinforcing the relatively low degree of immunity induced by killed vaccine by subsequent injection of living virus is that usually followed in vaccination against distemper in dogs. The possibilities of this procedure have not been extensively explored in the prophylaxis of human virus infections, although Pasteur's method of antirabies inoculation was based on the same principle.

Secondary reactions.—Recently, severe allergic reactions have been reported following injections of typhus and influenzal vaccines prepared from chick embryos (Hampton, 1947; Curphey, 1947). Serological studies have shown that such vaccines contain a variable proportion of egg protein. These findings suggest the need for inquiry into a history of sensitivity to egg protein and, when indicated, for skin testing before injecting such vaccines. However, typhus and influenza vaccines of this type have now been used extensively in man and severe reactions are probably no more common than the injection of therapeutic sera and other foreign proteins invokes. Recent work on rinderpest vaccines has indicated that an excess of chick embryo protein in inactivated vaccines of this kind may prevent an immune response to the virus antigens present (Maurer *et al.*, 1946). These observations emphasize the desirability of removing associated animal protein as completely as possible from virus vaccines.

THE PRESENT POSITION IN PARTICULAR DISEASES

Smallpox.—The proposed abolition of compulsory vaccination in this country does not indicate a lack of faith in the value of vaccination as a means of protection against smallpox. Vaccination is an essential measure in protecting a community from a threatened outbreak; revised notes on procedure have recently been published by the Ministry of Health (1947). The living vaccine used is prepared in this country from artificially infected calves or sheep, but in America vaccinia virus grown in tissue culture or in chick embryos has also been successfully used.

Yellow fever.—As stated above, the vaccine used is a living attenuated virus grown in chick embryo tissue. Although mosquito control offers an effective means of preventing yellow fever in urban communities this measure is not practicable in dealing with the rural form of the disease (jungle yellow fever). It is against yellow fever of this latter type that the present method of preventive inoculation with attenuated living vaccine has achieved notable success (Bugher and Gast-Galvis, 1944).

Rabies.—In this country the quarantine regulations have been effective in preventing the spread of rabies in canines. Recently the value of giving antirabies vaccine to persons bitten by rabid animals has been questioned,

this procedure. Living psittacosis virus has been injected subcutaneously in an attempt to protect laboratory workers whose work exposed them to grave risk of infection (Rivers and Schwentker, 1934). The method has recently been tried against mumps in men exposed to epidemic risk by intradermal injection of blood from acute cases of the disease (Leineberg, 1945). Virulent virus has also been used in veterinary medicine, immune serum being injected at the same time to lessen the risk of inducing serious disease. Whilst the injection of virulent virus by these methods may produce effective immunity it is too hazardous and uncertain for general use and has been discarded.

The use of *living attenuated vaccines* has so far given the most satisfactory results in the prophylaxis of virus infections by active immunization. Attenuation of virus for human inoculation may be achieved by continued passage of a virus through an animal species which does not naturally suffer from infection with it. Increase in virulence for such an animal host may be associated with a decrease in virulence for human beings. It is likely that the fixed virus of rabies after repeated passage through rabbits is less virulent for man than street virus, although direct proof of this is lacking (Zinsser, 1941). Attenuation may also be effected by continued growth of virus in tissue culture or in developing chick embryos. The attenuated vaccine now used in the prevention of yellow fever is prepared from virus propagated in chick embryo tissue. The efficacy of living vaccines of attenuated viruses against smallpox and yellow fever probably depends upon the fact that they produce mild infection with multiplication, and possibly dissemination, of the virus throughout the body, with consequent general stimulation of the antibody-forming mechanism. After vaccination the vaccinia virus usually generalizes although lesions other than in the skin at the site of inoculation are not as a rule apparent (Russell, 1941). Living attenuated vaccines prepared from allantoic fluids from infected chick embryos have also been given by intranasal spray in prophylactic trials against influenza (Burnet, 1943). Similar attenuated chick embryo vaccines are under investigation against mumps, measles and rinderpest.

Inactivated vaccines are generally prepared by treating virus suspensions with formalin, phenol, chloroform, ultra-violet light or other means. This type of vaccine is obviously safer than the other two and consequently would be preferable if its use were found to be followed by a satisfactory degree of immunity. For long it was believed that effective immunity could not be produced by inactivated vaccines and it seems that their efficacy varies with different viruses and the method of inactivation (Bedson, 1937). There is now no doubt that certain inactivated virus vaccines induce resistance to infection in experimental animals, as was demonstrated years ago with formalized herpes and psittacosis viruses (Bedson, 1931, 1933). One of the difficulties in the past has been to obtain a sufficient amount of virus antigen in killed vaccines prepared from crude suspensions of infected animal tissue. The development of improved methods of propagating

After a critical consideration of many papers on the subject, the Council of Pharmacy and Chemistry and the Council on Industrial Health in America reached the conclusion that "vaccines for colds cannot be recommended for routine administration to industrial groups or to individuals" (Status Report, 1944).

Infectious hepatitis.—The trials with gamma globulin in passive immunization against this disease have been referred to above. Owing to the difficulty of infecting animals with the causal virus, vaccines have not been prepared.

Poliomyelitis.—No effective means of passive or active immunization are at present available. Latent infections so greatly outnumber clinical cases during outbreaks that general immunization, even if possible, would not appear to be a practicable proposition.

Encephalitis.—The possibilities of providing effective vaccines against various forms of acute encephalitis are being explored in America, where these infections have been more prevalent than in Britain.

CONCLUSION

Although immunization against virus diseases has been established as a successful measure in only a few instances, the possibilities are by no means exhausted. The development of newer techniques for the preparation of potent vaccines and antisera is going forward, and in due course the results will be applied to the control of virus infections of man and animals.

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but the importance of vaccination in the control of rabies in dogs has been stressed in America, where canine infection is not uncommon (Committee Report, 1947). The vaccines available are prepared from the brains of rabbits which have been infected with fixed virus; the virus is inactivated by the addition of formalin, phenol or chloroform. A single injection of chloroform-treated virus seems to produce a high degree of immunity in dogs (Johnson and Leach, 1942).

Influenza.—The prospects of successful prophylaxis by active immunization are complicated by the fact that antigenically different strains of virus may be responsible for outbreaks at different times; the recent work of Hirst (1947), however, indicates that strain differences are probably much less than has been generally believed. Furthermore, individuals who have recovered from one attack have been shown to be susceptible to experimental infection with the same virus strain a few months later (Francis *et al.*, 1944). The extensive trials made in recent years of highly concentrated egg-grown, formol-inactivated vaccine prepared from several virus strains showed that, if inoculation is practised just before an expected epidemic prevalence, the incidence of infection may be reduced to a third or less of that which occurs in the non-vaccinated members of the same community (Commission on Influenza, 1944). The method is still under trial.

Measles.—The method of passive immunization of contacts with convalescent or pooled adult serum is that generally practised. Complete protection can be attained in the majority of exposed children if the serum is injected intramuscularly within a few days of exposure. A modified attack of the disease which, by conferring more durable active immunity may often be preferable, is likely to follow a smaller dose of serum or the usual dose given later, between the fourth and ninth day after exposure. Trials of a living attenuated measles vaccine prepared from virus grown on the chorio-allantois of chick embryos have been reported from America (*Lancet*, 1944) but this vaccine is not yet ready for general use.

Mumps.—Vaccines made from this virus have proved effective against the experimental disease in monkeys (Habel, 1946), but trials of a formalized vaccine prepared from parotid glands of infected monkeys gave only partial protection to children (Stokes, *et al.*, 1945). A living attenuated virus vaccine is under trial in America (*J. Amer. med. Ass.*, 1947). Mumps is not usually so serious as to justify general prophylactic immunization of children.

Chickenpox and herpes zoster.—Even if it were desirable to attempt specific immunization against these diseases, the preparation of a virus vaccine is not practicable as no means are yet available for obtaining virus by infecting animals or by other experimental procedures.

The common cold.—Although research on this troublesome complaint is in progress no means of specific immunization are at present available. The "vaccines" advertised are bacterial vaccines the use of which may lessen the secondary infection which is liable to complicate the initial virus attack, but they can have no prophylactic effect against the virus infection.

the hydrophobia appeared". Cocklebar (*Xanthium spinosum* Linn.) and, in Wales, dried and powdered scarlet pimpernel (*Anagallis arvensis* Linn.) were used within living memory for rabies. Zoster was treated by local applications of cat's blood.

Most virus infections are self-limiting: the patient either dies comparatively rapidly or else recovers, and even in such a disease as rabies it is by no means certain that all dogs that bite are rabid, or even that all rabid dogs necessarily transmit infection by their bite.

Many of the indigenous remedies used for virus infections are magical in origin. The yellow fruit of the barbary, the yellow flowers of Cassia, and the yellow dye turmeric are obviously sympathetic remedies for jaundice. Sir Thomas Browne (1646), however, had another explanation. He believed that

"The Devil deludeth us by . . . many superstitions in the cure of common diseases; seconding herein the expectation of men with events of his own contriving. Which some, unwilling to fall directly upon Magick, impute into the power of imagination".

Not all folk remedies can be dismissed as necessarily without value, for certain of them contain antibiotics. Garlic has already been mentioned; in addition, an antibiotic has recently been isolated by Robbins *et al.* (1947) from *Cassia reticulata*. Some folk remedies may thus be therapeutically active, if not against the actual viruses, at least against some of the secondary bacteria which accompany so many virus infections.

THE SULPHONAMIDES

The first specific chemotherapy of virus diseases had to await the discovery of the sulphonamides, although some believed that antimony salts had a specific action on lymphogranuloma venereum (Schmidt and Peter, 1938; Law, 1943). In experimental infections in mice, however, Andrewes, King and Van den Ende (1943) found antimonials (tartar emetic, anthiomaline and stibophen) quite inactive. Any action by antimony preparations in lymphogranuloma venereum is non-specific and equivalent in effect to intravenous injections of typhoid vaccines. The action of the sulphonamides is particularly seen in the psittacosis-lymphogranuloma group of viruses. This group includes the lymphogranuloma venereum virus, psittacosis and ornithosis viruses, trachoma, inclusion conjunctivitis or inclusion blennorrhœa, mouse pneumonitis of Nigg and Eaton, and cat pneumonia of Baker. They are distinguished from other viruses by the possession in common of certain characteristics.

(1) Large size: by direct measurement with the light or electron microscope, they are from 200 to 400 m μ in diameter whilst the smallest filterable forms are 150 to 250 m μ in diameter. (2) They can be stained differentially by the method of Castaneda or Macchiavello; they stain more readily than other viruses. (3) By means of the electron microscope they appear as spherical or hemispherical bodies with a limiting membrane (Rake *et al.*, 1946; Hamre *et al.*, 1947). (4) They contain thymonucleic acid (Lépine and Sautter, 1946). (5) When multiplying they undergo a regular sequence of morphological changes. (6) By complement fixation the psittacosis virus, lymphogranuloma venereum and pneumonitis viruses exhibit evidence of some antigenic similarity.

THE CHEMOTHERAPY OF VIRUS INFECTIONS

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As viruses are responsible for many of the commonest and most widespread of all the infectious diseases of animals and man it is not surprising that many attempts should have been made to find specific drugs for their treatment. The folk medicine of all peoples contains remedies for such diseases as the common cold (Fabricant, 1945), warts, infective hepatitis, and even rabies.

FOLK REMEDIES

The common cold has been treated with innumerable drugs, from pine and honey (Browne, 1646) to patulin, all of which have so far been found valueless (Stuart-Harris *et al.*, 1943; Medical Research Council, 1944; Robbins, 1944). Garlic (*Allium sativum* Linn.), from which an antibiotic has now been isolated (Cavallito and Bailey, 1944), has long enjoyed a reputation in the treatment of influenza. "The Regimen of Salerno", which certainly antedates the thirteenth century, states that the bark of "greene willow destroyeth warts" (Harington, 1608); more recently Semon (1933) recommended strong salicylic acid plasters, up to 60 per cent. strength. The latices of the Mexican or prickly poppy (*Argemone mexicana* Linn.), and of *Euphorbia lateriflora* Schum. and Thonn, are used with success in the treatment of warts by West African tribes.

Jaundice also has had many treatments. In England barberry bark (*Berberis vulgaris* Linn.) and the roots and leaves of the buckthorn plantain (*Plantago coronopus* Linn.) are still used as folk remedies, whilst in Africa the leaves of *Cassia occidentalis* Linn. have a high reputation in the treatment of infective hepatitis and yellow fever.

Rabies was treated by Galen with a daily dose of one drachm of burned powder of river crabs, but, as Shakespeare noted, "The most sovereign prescription in Galen is but empiricute". For those who preferred polypharmacy there was a famous *Decoctum ad morsum canis rabidi* consisting of rue, garlic, London or Venice treacle, and filings of pewter boiled in ale. This had to be taken by mouth for nine days and was even superior to the liver of the mad dog itself. "The Regimen of Salerno", as translated by Sir John Harington (1608), advised that

"If your hound by hap should bite his Master
With Honey, Rew and Onyons make a plaster".

A century and a half later Joseph Dalby (1762), a well-known surgeon of Birmingham, claimed that by means of cinnabar and the finest musk he had succeeded in curing "upwards of a hundred cases, whereof two were after

followed by 3 gm. for twenty days (a total of 66 gm.) usually produces rapid improvement (Hebb *et al.*, 1939; Stein, 1940; Coutts, 1943; Noojin, Callaway and Schulze, 1943). Cases of rectal stricture and chronic ulceration of the vulva with urethritis were first treated by Shropshire (1938). Some observers have obtained amelioration even of cases of elephantiasis of the vulva and of fibrous rectal strictures: surgical measures may have to be used in some of these cases (Kampmeier and Larsen, 1942; Pettavel, 1943; Woods and Hanlon, 1944).

The Frei cutaneous reaction does not become negative immediately on the disappearance of the clinical signs and symptoms following sulphonamide treatment. Heyman *et al.* (1947) were, however, unable to isolate the virus from the lymph nodes for longer than two to three months after the cessation of treatment, but in one patient who relapsed six months after receiving a total of 120 gm. the virus was found to be present in the involved lymph nodes. Sonck (1943) noted that the administration of nicotinic acid amide during treatment of proctitis due to lymphogranuloma venereum apparently inhibited the action of the sulphonamide. Hyperproteinæmia is usually associated with lymphogranuloma venereum infection but if sulphonamide treatment is begun at a very early stage of infection this change may not be noted (Schamberg, 1941; Heyman, 1946).

Conjunctivitis due to lymphogranuloma venereum virus may occur as a primary lesion or as a secondary manifestation of previous genital disease. A few cases have been treated with sulphonamides.

Curth, Curth and Sanders (1940) reported a patient with kerato-conjunctivitis of six years' duration simulating Parinaud's conjunctivitis. Although useful vision was lost from corneal cicatrization all inflammatory signs disappeared following sulphanilamide by mouth over a period of four months. A laboratory worker was accidentally infected: an acute conjunctivitis did not respond to the usual forms of therapy but healed completely after 3 gm. of sulphadiazine daily for ten days (Oliphant, Powell and Perrin, 1942). A corneal ulcer which was probably due to the virus of lymphogranuloma venereum improved rapidly under sulphanilamide (Meyer and Reber, 1941). MacNie (1941) reports two cases in which sulphonamides were of value in clearing up uveitis and kerato-conjunctivitis due to lymphogranuloma venereum.

Psittacosis.—Mauer (1938) found that about 50 per cent. of mice infected with psittacosis could be saved by treatment with acriflavine. These results have not been confirmed, but nitroacridine 3582 is of value (Hurst, 1947). Psittacosis is only rarely affected by sulphonamides in mice (Rudd and Burnet, 1941), and clinically in man there is not much evidence that sulphonamides are of value (Meiklejohn *et al.*, 1944; Levinson *et al.*, 1944). Hinshaw (1940), however, believed that one patient was cured by sulphapyridine. Some strains of psittacosis are nevertheless affected by sulphonamides. Strain 6 BC, both in mice (Wiseman *et al.*, 1946) and in chick embryos (Meiklejohn *et al.*, 1946), is susceptible both to sulphadiazine and penicillin: 19 of 22 mice survived when given sulphadiazine in the food to the extent of 0.5 per cent. by weight of the food for fourteen days after exposure to the virus; 26 untreated controls all died. Rosebury *et al.* (1947)

It is this virus group which Rake (1948) has termed the Chlamydozoaceæ. *Lymphogranuloma venereum*. The first successful use of the sulphonamides was by Gjurić (1938) who obtained rapid resolution of the inguinal buboes by the injection of stibophen and the administration of prontosil by mouth; the latter drug was given in daily doses of 2.5 gm., followed by 2 gm. daily for three days; after a rest of three days the course was repeated. A little later Kubitzki (1938) and Montel and Nguyen-Van-Tho (1938) obtained similar results. When prontosil alone was given by mouth and by injection prompt fall in temperature and improvement of the local lesions occurred.

Levaditi (1938a) in the meantime had found that the buboes produced by lymphogranuloma venereum virus in the groins of guinea-pigs were rapidly cured by sulphanilamide and sodium 4-sulphamidobenzeneazo-3':5'-diaminobenzoate. The buboes produced in guinea-pigs, however, occur so irregularly and are so rapidly resolved that no accurate estimate of therapeutic efficiency can be made in these animals. In infections in mice in which the virus is injected directly into the brain, sulphanilamide caused a retardation in the development of symptoms and in some cases the lives of the mice were saved (Bär, 1938; MacCallum and Findlay, 1938; Levaditi, 1938b). The lesions in treated mice are smaller than in untreated animals but the virus in the brain is not destroyed by sulphonamides. In one instance Jones, Rake and Stearns (1945) isolated virus from mouse brain one year after treatment. The effect of the sulphonamides on lymphogranuloma venereum virus is thus analogous to that of chemotherapeutic drugs on small protozoa such as *Babesia* and *Coccidia*.

There is now general agreement that all sulphonamides and sulphones have some action on the virus (Jones, Rake and Stearns, 1945; Andrewes, King and Van den Ende, 1943; Levaditi *et al.*, 1944), although owing to differences in the strain of virus used, in the mode of inoculation of the virus in the animal host (intracerebral, intranasal or in the developing chick embryo), and in the dosage and method of administration of the drug, variations in the order of effectiveness of the sulphonamides have been recorded (Findlay, 1940a; Jones, Rake and McKee, 1941; Van den Ende and Lush, 1943; Felton, Hebb and Oliphant, 1942). Sulphadiazine and sulphathiazole are among the more active compounds, whilst good results have been obtained both in man and mice with sulphamezathine and sulphamerazine, as well as with the sulphones (MacCallum and Findlay, 1938). Although the protection is not as marked as in the case of bacteria, *p*-aminobenzoic acid appears to inhibit the action of the sulphonamides (Findlay, 1940b; Levaditi and Perault, 1942; Mudrow and Bock, 1943; Rodaniche, 1943); in addition, the sulphonamides have no *in vitro* killing action (MacCallum and Findlay, 1938; Schlossberger and Bär, 1939; Rodaniche, 1943). A few workers, however, have put forward contrary views on these findings (Holder, Levine and Bullowa, 1942; Seeler, Graessle and Dusenberger, 1943). Holder *et al.* (1942), for instance, believe that *in vitro* contact of sulphonamides may slightly attenuate the virus: it seems, however, that in these experiments some sulphonamide must inevitably be inoculated with the virus. The lymphogranuloma venereum virus when injected intravenously in high concentration kills within thirty-six hours by what has been termed, on somewhat slender evidence, a "toxic" effect. Such toxic deaths are not prevented by sulphonamides (Rake and Hamre, 1944). According to Wall (1947) mice given a sulphonamide after infection but before symptoms appear do not develop complement-fixing antibodies; those given a sulphonamide after the appearance of symptoms have low titres which can be still further reduced by long-continued treatment. So far experiments by Rodaniche (1943) and in my laboratory have failed after more than twenty passages to produce a sulphanilamide-fast strain of the virus. Many other drugs appear without action on the lymphogranuloma venereum virus (Andrewes, King and Van den Ende, 1943).

In man, more especially during the acute stage, sulphonamides act rapidly if given in sufficient doses. In early cases 6 gm. on the first day

fectured tissues to sulphonamides for periods up to five hours does not destroy the infectivity for monkeys. In patients treated with sulphonamides in West Africa inclusion bodies and infectivity for monkeys disappeared after five to seven days of treatment.

Although sulphapyridine, sulphanilamide, sulphanilic acid derivatives (Cosgrove and Hundley, 1942), sulphathiazole, sulphamerazine (Neil, 1947) and sulphadiazine are all curative, Richards (1943), who has had experience with more than 4000 Red Indians treated by sulphonamides, finds sulphadiazine the best. Whilst small doses, such as 1.3 gm. daily for seven weeks, may produce cures it is preferable to give sulphonamides in sufficient dosage to produce a blood level of 3 mgm. per 100 c.cm. for as long as the cornea shows any signs of active disease. If local therapy is to be employed, a hydrous wool fat petrolatum base with 5 or 10 per cent. sulphathiazole probably permits the longest persistence of the sulphonamide in the conjunctival sac. The use of a 15 per cent. sodium sulphacetamide collyrium may be of value (Alvaro, 1945). Thygeson (1943) believes that only when severe secondary infection, particularly of the lid margins, tear deficiency, or trichiasis is present, is supplementary treatment required.

Inclusion conjunctivitis.—The first report of the successful treatment of inclusion conjunctivitis with sulphonamides was made by McKelvie (1938) in Khartoum. Later reports on the rapid cure of the condition came from Thygeson (1939, 1941), Giddens and Howard (1940), Braley (1942), Thygeson and Stone (1942), and Thygeson and Braley (1943). Only Lugossy (1940) recorded equivocal results. Sulphanilamide, sulphathiazole, and sulphadiazine have all been given by mouth and successful cures have been obtained in a very short time. Thygeson and Stone (1942) find that local therapy alone is not as satisfactory in adults as in small infants, possibly because in the newborn the lachrymal glands are scarcely functioning. In 11 cases of inclusion blennorrhœa of the newborn, Thygeson and Stone obtained cures by the local application of 5 per cent. sulphathiazole ointment six times a day; recovery was almost as rapid as with oral therapy. Thygeson (1943) suggests that more frequent local therapy in adults is likely to be of value. Vorisek (1947) recommends irrigation with a 5 per cent. solution of sodium sulphathiazole every two hours by day, the local application of sulphathiazole ointment at night, and sulphadiazine by mouth; this treatment can be relied upon to produce improvement in from seven to ten days, as compared with six weeks by older forms of therapy. Thygeson (1940) found the virus still infective for baboons after three, but not after five, days' treatment with sulphonamides. As inclusion conjunctivitis is rarely associated with secondary bacterial infection sulphonamides must presumably act directly on the virus.

Heart water of cattle.—Although the causal agent is usually described as a rickettsia (*R.ruminantium*), it should more properly be placed with the viruses. It responds to a sulphonamide, uleron, according to Neitz (1940).

Infectious kerato-conjunctivitis of cattle, although also said to be due to a

find that another classical strain, "Gleason", is also sensitive to sulphadiazine. A pigeon ornithosis virus, strain St, isolated from a case of pneumonitis in the Bayou region of Louisiana by Olson and Treuting (1944) and a meningo-pneumonitis virus (Cal. 10) were unaffected by sulphadiazine.

Pneumonitis.—Sulphonamides inhibit infections in mice with the virus of mouse pneumonitis (Rake, Jones and Nigg, 1942), but infections with the agents of feline pneumonitis and meningo-pneumonitis are scarcely affected (Rake, Jones and Nigg, 1942; Rake and Hamre, 1944). In mice, hamsters, rats and cotton rats, and in yolk-sac infections of chick embryos, sulphamerazine was found to inhibit pneumonitis infection in all species, although smaller doses were required in the mouse than in the hamster (0.0025 mgm. per gm. of body weight in mice and 0.1 mgm. per gm. in hamsters). With the agent of feline pneumonitis large doses of sulphamerazine, near the toxic limit, caused moderate inhibition of the lung lesions in hamsters and white rats, slight inhibition in cotton rats, and no effect at all in mice and chick embryos (Eaton and Hanford, 1945). Mudrow and Bock (1943) find that *p*-aminobenzoic acid inhibits the action of sulphapyridine on the mouse pneumonitis virus.

Trachoma.—In 1938, Lian and Dik in the East Indies, Loe in America, and Kirk, McKelvie and Hussein Ahmed Hussein in the Anglo-Egyptian Sudan reported that prontosil and sulphanilamide are of value in trachoma. Sulphonamides by mouth rapidly improved the conjunctivitis and corneal thickening, whilst corneal complications such as pannus, keratitis and ulcer cleared up and showed little tendency to recur. Photophobia and continuous lachrymation were also greatly lessened. Since then many observations have been made on the effects of sulphonamides on trachoma. Extensive reviews have been published by Thygeson (1943) and Poleff (1943). A certain number of workers regard sulphonamides as of little value, with no specific action on the virus, any possible therapeutic effects being due to action on secondary bacteria. A much larger group, however, believe that sulphonamides produce a considerable percentage of complete and permanent cures, thus representing an important advance in the treatment by chemotherapy.

It is not easy to account for the failures with sulphonamides: in some cases the diagnosis may have been at fault, in many the dosage and the duration of treatment were obviously inadequate. Secondary infections and such factors as a deficiency of tears, trichiasis or xerosis may play a part in preventing cure. It is noticeable that many failures have been reported from Egypt where the strain of trachoma virus is highly virulent. In West Africa, on the other hand, trachoma is comparatively mild and there are few failures with sulphonamides. Thygeson (1943) insists that all cases treated should be carefully classified. In cases in which there is conjunctival scarring or much pannus the lesions may not clear up, for they may be due to pemphigus, surgical intervention, or other factors.

Julianelle and Smith (1942) find that exposure of trachoma virus in in-

Psittacosis virus.—The curative action of penicillin on ornithosis and psittacosis viruses in mice was first demonstrated by Heilman and Herrell (1944a, b), and Parker and Diefendorf (1944), and confirmed by Bedson and May (1945). In human beings infected with an ornithosis virus Turgasen (1944) and Ford and Kispert (1945) reported cures by means of penicillin, whilst Flippin, Gaydosh and Fittipoldi (1945) and Reinmann (1945) cured human cases of psittacosis with penicillin. Rosebury *et al.* (1947) also reported the dramatic recovery of a patient infected with the 6 BC strain of psittacosis.

Penicillin therapy was begun on the fourth day of illness with 50,000 units intramuscularly every three hours, or 400,000 units a day. On the following day sulphadiazine was given at the rate of 6 gm. a day. After the patient had been on penicillin for thirty-six hours and sulphadiazine for eighteen hours his temperature fell and remained normal. Penicillin was continued until the fourteenth day with a total of 3,900,000 units; sulphadiazine was given from the fifth to twelfth days, a total of 48 gm.

More recently there has been described a single case of infection due to an ornithosis virus which recovered promptly after the initiation of penicillin therapy. Few comparisons have been made of the relative effectiveness of penicillin and the sulphonamides.

Against psittacosis strain 6 BC, which in mice and chick embryos reacts to both penicillin and sulphadiazine (Wiseman *et al.*, 1946; Meiklejohn *et al.*, 1946), Early and Morgan (1946 a, b) found that penicillin and sulphadiazine were equally effective when psittacosis virus was injected into mice by intravenous and intraperitoneal routes. If the virus was given intracerebrally or intranasally, penicillin was less effective than sulphadiazine. Streptomycin had no effect on this strain in mice, nor did *p*-aminobenzoic acid, which is effective against rickettsiae.

The meningo-pneumonitis virus also is susceptible to penicillin both in chick embryos and in mice (Parker and Diefendorf, 1944).

Trachoma.—Insufficient information is as yet available to assess the value of penicillin in trachoma. Keyes (1944) applied 1000 units per c.cm. locally every two hours for nine days while the lesions progressed. Sorsby (1945b) cured one recent case but two cases of longer standing remained unaffected. The most hopeful results are those of Darius (1945).

Inclusion conjunctivitis.—Eight cases were treated with penicillin locally by Sorsby (1945a) with excellent results; one case relapsed.

THE CHEMOTHERAPY OF THE POX VIRUSES

The pox viruses include smallpox and alastrim of man, vaccinia and the mammalian pox viruses and the various avian viruses of fowl, pigeon and canary-pox. Until recently there was little evidence of any direct chemotherapeutic action on this group of viruses. In hæmorrhagic smallpox the administration of sulphonamides by mouth, more especially sulphathiazole and sulphadiazine, tends to decrease the mortality by controlling the secondary bacterial organisms, especially streptococci and staphylococci, which are responsible for so many of the complications (Patel and Naidu, 1940; Cottrell and Knight, 1943; Leishman, 1944). Sulphadiazine is the

rickettsia, should rather be grouped with the viruses. Sulphathiazole, given for five days intravenously twice daily, cured 8 cattle in from fourteen to eighteen days. Virus bodies still persisted in the conjunctiva at the end of treatment (Götze, 1945). The epidemic kerato-conjunctivitis of the Middle East described by Feigenbaum *et al.* (1945) is due to a virus but is not affected by the sulphonamides or penicillin.

ANTIBIOTICS AND THE PSITTACOSIS-LYMPHOGRANULOMA VIRUSES

Just as certain of the viruses belonging to this group are sensitive to the sulphonamides so also they have been found to react to certain antibiotics.

Lymphogranuloma venereum.—Andrewes, King and Van den Ende (1943) reported that penicillin was inactive against the virus of lymphogranuloma venereum when it was inoculated intranasally or intracerebrally in mice; penicillin, however, suppressed the growth of the virus in tissue culture. Levaditi and Vaisman (1943, 1945) found in mice that very large doses of penicillin, such as 1,000,000 units per kgm. of body weight given intraperitoneally, will not only protect against intracerebral inoculation of the virus but will also lead to destruction of the virus in the brain. Rake and Jones (1946) have independently obtained similar results.

When penicillin is given in large doses intraperitoneally to mice infected intracerebrally with the virus of lymphogranuloma venereum, convulsions, spasticity, and death occur in a considerable number of animals. Provided the mice do not die from the local effect of penicillin on the central nervous system some protection is obtained against intracerebral infection with doses equal to about 7,700 Oxford units per kgm. of body weight in one day; after intranasal infection a dose of about 30,000 units per kgm. per day produced a slight therapeutic action. At high concentration, penicillin of low purity was found to exert an action on the agent *in vitro*. Heilman (1946) gave subcutaneous doses to mice of 1000 units daily in 0.05 c.cm. of 4.8 per cent. beeswax in sesame oil, for seven days. Of 41 treated mice inoculated intracerebrally, one died of pneumonia on the twenty-ninth day and two developed hydrocephalus, but of 41 controls, 34 died in from two to twenty-three days and only 7 survived. Virus was not destroyed in the brain.

Reports of the clinical application of penicillin in lymphogranuloma venereum are as yet few. Earlier results were variable.

Morginson (1945), for instance, treated 3 cases with 1,625,000, 1,800,000 and 4,675,000 units; the first case had proved refractory to sulphonamides. Kile (1945) failed in 8 cases (doses unspecified). Willcox (1946), however, in a series of 25 early cases in West African soldiers, which I was able to follow, obtained striking results with the injection of penicillin in oil: of 10 cases given 100,000 units in a single injection, 5 cleared up in an average of 6.1 days. Fifteen patients were given 100,000 units in saline followed by 100,000 units in oil three to four hours later; 10 cleared up in five days; 2 relapsed and 1 failed. Two European patients received 1,000,000 units in saline, 40,000 units being given three-hourly for three days. Improvement began after twenty-four hours and the patients were discharged from hospital after four and six days.

Mayne and Bain (1947) have recently emphasized the value of penicillin in treating chronic discharging sinuses from a lymphogranuloma venereum bubo; here the action of the penicillin appeared to be on *Staphylococcus aureus* rather than on the virus.

and Manwell (1941) in canaries. Robbins (1942), in observations which lack confirmation, has claimed that quinine benefits fowl-pox infection in chicks, whilst Jones *et al.* (1945) found that actinomycin A, which is very toxic, had a slight *in vitro* action on fowl-pox and on tracheo-bronchitis virus.

Warts.—Many hundreds of different treatments have been reported for warts. Most of them are of no more value than the "spunk water" which Tom Sawyer collected in fear and trembling from a graveyard at dead of night. Recently a new therapy has been attempted for condylomata acuminata.

Kaplan in 1942 treated 20 patients with 25 per cent. podophyllin in mineral oil: rapid cures were obtained. Later, Culp and his associates (1944 a, b) gave details of 100 additional cases; all the patients were males: 97 had penile, 2 anal, and 1 perineal warts. Of the penile cases 62 were treated with 25 per cent. podophyllin in oil and 35 with a crude podophyllin paste made with water. Of the first group, 56 were cured by one application, 5 by two applications and 1 by three applications. The usual time for cure was two to three days, but in one case sixteen days were necessary. In the second group only two required a second course of the aqueous paste. Six of the 35, however, had an acute balanitis. This balanitis is due to the fact that podophyllin contains podophyllotoxin which is converted by alkalis into podophyllic acid. To overcome the possibility of balanitis Haber (1945) cleansed the penis with eusol and covered the glans with zinc ointment; he then applied 5 per cent. podophyllin in powdered tannic acid. In 35 cases the average duration of treatment was four to five days, the shortest being eight hours.

Acute urethritis is not a contraindication. MacGregor (1945) also used podophyllin with success. Finkle and Frishwasser (1947) find that balanitis may be avoided if podophyllin is applied for not longer than five hours; if the period of application is only three hours, warts invariably recur. King and Sullivan (1946) used colchicine in oil in place of podophyllin with good results on condylomata acuminata. On the common warts of the hands neither podophyllin nor colchicine has any action, probably because of the thick horny layer which protects the infected cells. At present there is no evidence that podophyllin and colchicine have any direct action on the warts virus. As Sullivan and Wechsler (1947) have pointed out, podophyllin affects the dividing cell in late prophase, the spindle mechanism being involved and chromosomes dispersed throughout the cell. Up to metaphase there is an increased number of mitotic figures: later there is a decrease and a complete absence of anaphase and telophase figures.

For some years the bismuth treatment of warts has been advocated, a 1.5 per cent. aqueous solution of bismuth sodium tartrate being injected into the base of the warts (Brown and Erdos-Brown, 1938). Such treatment can, however, give rise to severe local and general reactions (Cameron, 1947).

Molluscum contagiosum.—There is some evidence that sulphonamides may be of value in the treatment of molluscum contagiosum.

In 1941 Sommerville reported eight cases in which the patient had been treated with sulphapyridine. In six the lesions cleared under sulphapyridine, whilst in two others toxic reactions occurred. Four patients who took 2 to 4 gm. daily were cured in two to eight weeks; two who failed to respond with a daily dose of 1 gm. cleared rapidly with 2 gm. daily. Of the six patients who were cured, five were children ranging in age from nine months to fifteen years. Hill and Downing

most satisfactory sulphonamide; sulphathiazole is superior to sulphapyridine (Osborne, 1945). In West Africans infected with varicella under unhygienic conditions sulphonamides are also of value.

Andrewes, King and Van den Ende (1943) tested 74 compounds, including penicillin, against vaccinia virus without effect. Ramon *et al.* (1947) found that crude filtrates of cultures of *Bacillus subtilis* incubated at 37° C. with vaccinia virus completely inactivated the virus. Crude filtrates of *Actinomyces griseus* and *Penicillium notatum* had a less pronounced action on the virus. The majority of observers, following Andrewes *et al.* (1943), have found pure penicillin to be devoid of action on vaccinia in the rabbit (Neter and Will, 1944; Parker and Diefendorf, 1944; Neter, 1945; Kolmer and Rule, 1946; Ramon and Richou, 1946; Morin and Turcotte, 1947; Fasquelle, 1947). In view of these negative findings pure penicillin has been added to crude vaccinia pulp to destroy contaminating bacteria. (In Russia the use of Soviet gramicidin has been recommended by Marchenko and Rakhman (1946) for the same purpose.) Robbins (1944) found that penicillin and patulin were without action on fowl-pox in chicks. Recently, however, Gohar and Bashatli (1946) have brought forward evidence that penicillin may cure vaccinia in the rabbit.

Rabbits were given 1000 units three-hourly for three days to a total of 24,000 units. The first injection was given either immediately after inoculation of the virus or one, two, three and four days later. When therapy was delayed for two days or longer there was no effect, but when treatment was begun up to one day after inoculation the skin lesions were trivial. If treatment with penicillin was continued for three days only, lesions appeared two days later, but if treatment was continued for five days, a total of 40,000 units, no lesions appeared after cessation of treatment. Local application of penicillin was of some slight value.

Somewhat similar results have been obtained by Fust and Grünig (1946). When penicillin and vaccinia virus were first mixed and the mixture subsequently inoculated intradermally into rabbits the lesions were almost completely inhibited. More remarkable, however, was the finding that boiling the penicillin solution for fifteen minutes enhanced the effect, although this treatment destroyed about half its antibiotic activity.

A possible clue to this seeming anomaly is to be found in the experiments of Groupé and Rake (1947).

Using the chorio-allantoic membrane of the developing chick embryo it was found that vaccinia, canary-pox and fowl-pox viruses were completely inhibited by 3,750, 7,500 and 15,000 units of commercial penicillin when the virus was mixed with the penicillin and incubated *in vitro* for two hours at room temperature. An impurity, or impurities, in commercial penicillin rather than penicillin itself appears to be responsible for the inhibition, for the inhibition is not decreased when aqueous solutions of commercial penicillin are heated at 100° C. for ten minutes. Normal egg white inhibited the antiviral activity of commercial penicillin.

The antiviral substance in commercial penicillin is possibly *o*-hydroxy-phenylacetic acid (Fischbach *et al.*, 1947).

Mercurochrome also prevented the development of canary-pox virus on the chorio-allantoic membrane of the developing chick embryo, thus confirming the observations of Manwell and Goldstein (1939) and Coulston

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(1942) reported an adult with lesions which had continued for one year: after sulphapyridine had been given in doses of 2 gm. daily all the lesions except one cleared up within a week. Laymon (1946) gave a boy of twelve years a dose of 4 gm. daily: within a week the lesions had begun to regress and on reducing the dose to 2 gm. daily for a second week the lesions entirely disappeared.

THE CHEMOTHERAPY OF INFLUENZA

Among the numerous substances which have been found to act on rickettsiæ are penicillin, *p*-aminobenzoic acid (Grieff *et al.*, 1944), *p*-sulphamidobenzamidine (Andrewes *et al.*, 1944), forbisen and toluidine blue (Peterson, 1944), and other thiazine dyes (Andrewes *et al.*, 1946) such as 2-nitro-5-aminoacridine, "rutenol", and 2,3-dimethoxy-6-nitro-9-(diethyl-amino-oxypropyl) aminoacridine dehydrochloride or nitroacridine 3582 (Smadel *et al.*, 1946). The last also has an inhibitory action on influenza B (Lee strain) virus.

Green, Rasmussen and Smadel (1946) found that 0.5 to 1.0 mgm. of nitroacridine 3582 in 0.1 c.cm. of 0.9 per cent. sodium chloride solution, given by the allantoic route to chick embryos infected at the same time with from 1 to 10,000 minimal infected doses of virus, was sufficient to inhibit or delay the development of the virus, when the infecting dose was from 1 to 10 M.L.D., during a period of observation of forty-eight to seventy-two hours.

Nitroacridine 3582 has a similar but less pronounced effect on influenza A (PR8 strain) in developing chick embryos. Rutenol and mepacrine also have some viristatic action when tested against influenza viruses. Although nitroacridine 3582 is somewhat viricidal *in vitro* this is insufficient to account for the degree of inhibition observed *in vivo* (Rasmussen *et al.*, 1947).

Coggeshall and Maier (1942) and Krueger *et al.* (1943) tested numerous compounds against influenza without result. Andrewes, King and Van der Ende (1943) failed to observe any activity against influenza A among 115 compounds tested. Wheeler and Nungester (1944) believe that influenza is favourably influenced by atropine sulphate. If such an effect occurs, direct action on the virus is very doubtful.

The effect on influenzal infections in the mouse of some 24 antibiotic lactones and their analogues has been studied by Rubin and Giarman (1947) using the PR8 strain of influenza A virus. In addition to some members of the furan series, the following compounds had a definite therapeutic action: γ -butyrolactone; 6-methoxy-8-(2,5-dimethylpyrrol-1)-quinoline; 3-phenyl-2-butene-1,4-olide; 3-methyl-5-carboxy-2-pentene-1,4-olide; parasorbic acid and isoclavacin. The action of these compounds is the more impressive because they were not administered until the disease had reached a fairly advanced stage.

OTHER VIRUSES AND CHEMOTHERAPY

From time to time claims have been made that other viruses are susceptible to sulphonamides. As in the case of smallpox, the value of the sulphonamides or penicillin in influenza in man, in measles (Thompson and Greenfield, 1938; Hogarth, 1939; Anderson, 1939), in infectious mononucleosis with

angina (Stannus and Findlay, 1939) and in dog distemper (Groulade, 1937; MacIntyre and Buttle, 1938; Marcus and Necheles, 1938; Bryan, 1941) is due to action on secondary bacterial invaders.

No attempt will be made to discuss the inactivation of viruses *in vitro*. It may be noted that filtrates of *Bacillus subtilis* are said by Remlinger and Bailly (1946) to inactivate rabies virus with great rapidity at 38° C. Penicillin is without action on rabies. According to Sulkin *et al.* (1946) anaesthesia decreases susceptibility to western equine encephalomyelitis. Sodium iodide therapy is said to benefit equine encephalomyelitis (Radeleff, 1946). Trypan red and Congo red have been found by Wood and Rusoff (1945) to afford some protection against mice infected with virus. Thiouracil and thyroactive substances are said to decrease susceptibility to poliomyelitis virus (Holtman, 1946). *In vitro* experiments by Sulkin and Zarafonitis (1947) showed that anaesthetics have some action on rabies, poliomyelitis, St. Louis encephalitis and equine encephalitis viruses. Linhares (1944) claims that the neurotropic strain of yellow fever can be inactivated both *in vivo* and *in vitro* by filtrates of cultures of *Penicillium camemberti*, *Aspergillus flavus* and *Actinomyces* sp. A possible action of neoarsphenamine and other arsenicals in preventing infection with poliomyelitis has been demonstrated by McKinstry and Reading (1945). Numerous negative results have been reported with sulphonamides: yellow fever and Rift Valley fever (Findlay and MacCallum, 1938), poliomyelitis (Coggeshall and Maier, 1942; Kramer, Geer and Szobel, 1944; McKinstry and Reading, 1944, 1945), St. Louis encephalitis (Kramer, Geer and Szobel, 1944). Aspergillic acid has no action on equine encephalomyelitis (Sulkin and Goth, 1945).

Viruses are readily destroyed by oxidizing agents *in vitro*. Thurmon and Brown (1947) believe that a glycerite of hydrogen peroxide is of value when applied locally to the lesions of herpes simplex. Warts are unaffected.

No successful chemotherapy of a plant virus has yet been recorded. It is of interest, however, to note that many fungi and bacteria known to produce antibiotics have been found to inactivate plant viruses (Johnson and Hoggan, 1937; Johnson, 1938; Fulton, 1943). Penicillin is said to be without action on tobacco mosaic virus (Manil, 1947), but a substance, probably a polysaccharide, is said to inactivate it (Takahashi, 1946).

THE CHEMOTHERAPY OF BACTERIOPHAGES

The chemotherapy of bacteriophages is chiefly of interest because it provides a simple model for chemotherapeutic action in general which may be of value in understanding the mechanism of drugs on more complex organisms. Many substances have been found capable of inhibiting development of bacteriophage without greatly affecting the multiplication of the bacteria on which it lives. Stassano and de Beaufort (1925) and Bordet and Renaux (1928) showed that some phages are inhibited by dilutions of citrate and oxalate which do not affect the associated bacteria. Spizizen (1943) believes that arsenite is a specific inhibitor of a coli-phage. Fitzgerald

and Lee (1946) and Fitzgerald and Babbitt (1946) found that several acridines, and particularly "phosphine GRN", are capable of inhibiting the multiplication of a coli-bacteriophage at concentrations well below the bacteriostatic end-point. Jones (1945) observed that some bacteriophages are specifically inhibited by streptomycin. An analogue of tryptophane, 5-methyl tryptophane, can inhibit the multiplication of some strains of bacteriophage but only in concentrations which interfere with the growth of the bacterial host cells (Cohen and Anderson, 1946).

THE MODE OF ACTION OF CHEMOTHERAPEUTIC AGENTS ON VIRUSES

The difficulties inherent in the successful chemotherapy of viruses, in view of the fact that viruses are obligatory intracellular parasites with a metabolism intimately bound up with that of the cells of their hosts, have been emphasized by Findlay (1939), Mudd (1945), and Andrewes and King (1946). Chemotherapy is especially difficult in diseases such as yellow fever, in which the onset of signs and symptoms coincides with a disorganization of cell metabolism; here also in man the virus is specifically neutralized by the production of immune bodies within seventy-two hours of the onset of fever but the patient may die within a week owing to the necrotic changes already produced in the kidneys, heart and liver. Nevertheless, the finding of substances which can act specifically on rickettsiæ and on viruses of the psittacosis-lymphogranuloma group shows that the problem of dealing with obligatory intracellular parasites is by no means insoluble.

Several different paths are coalescing to form a broad highway which should lead to the successful chemotherapy of many virus infections. Ledingham (1926, 1927) showed that the intradermal injection of India ink into rabbits rendered the areas so injected refractory to the subsequent injection of vaccinia virus, presumably because the virus particles could not parasitize the reticulo-endothelial cells. In working with plant viruses Thung (1931) found that a feebly pathogenic strain of tobacco mosaic virus would inhibit the action of a highly pathogenic strain inoculated at the same time or shortly afterwards. McKinney (1929) obtained similar results, common tobacco mosaic interfering with the growth of yellow tobacco mosaic virus. Salaman (1933) reported analogous findings for strains of potato virus. A number of other examples of plant virus interference have now been recorded: information is summarized by Price (1940). The same phenomenon also occurs in relation to animal viruses. Some strains of herpes virus placed on the scarified cornea of the rabbit migrate along the optic nerve to the brain, causing encephalitis; other strains remain localized to the cornea. Magrassi (1935 a, b) showed that if the cornea were inoculated with a non-encephalitogenic strain the progress of an encephalitogenic strain to the brain was blocked. Hoskins (1935) showed that in monkeys inoculation of the relatively non-pathogenic neurotropic strain of yellow fever protected against injection of the virulent viscerotropic strain,

This result was confirmed and extended by Findlay and MacCallum (1938), who found that Rift Valley fever virus would protect monkeys against the viscerotropic yellow fever virus, whilst in mice the neurotropic strain of yellow fever virus would protect mice against Rift Valley fever virus, which is highly pathogenic for this species. These results have been confirmed by De Assumpção (1944) in rhesus monkeys and camodongos, whilst Dalldorf, Douglass and Robinson (1938) have shown that lymphocytic choriomeningitis virus will protect monkeys against poliomyelitis virus. These observations show that the phenomenon of virus interference is quite distinct from that of immunity, for the interfering virus need not be related antigenically to the virus with which it interferes. The hypothesis put forward by Findlay and MacCallum was that both viruses competed for the same receptor groups of susceptible cells; it was a case of "first come first served". Since then numerous cases of virus interference have been demonstrated either in animals or in tissue culture, even when the interfering virus is added some time after the virulent strain. Examples of interference between animal viruses are shown in table I (p. 123). The phenomenon also occurs between bacteriophages (White, 1937; Delbrück and Luria, 1942); in the last instance the process can be demonstrated under the electron microscope. Delbrück and Luria (1942) found that a bacteriophage inactivated by ultra-violet light could block the activity of an active bacteriophage. Similar results were reported by Henle and Henle (1943, 1944) and Ziegler and Horsfall (1944) for influenza, and by Andrewes and Elford (1947) for ectromelia. If, as Andrewes and King (1946) emphasize, the interfering principle which seems to reside in the killed virus particle could be isolated, chemically identified and imitated, new chemotherapeutic possibilities would be opened up. It is of interest to note that the idea of using a virus infection to eradicate another disease is of long standing. Winterbottom (1803) recorded that Africans in Sierra Leone were accustomed to treat chronic ringworm by inoculating the skin with herpes virus. Venereal warts may also be destroyed by infecting them with herpes.

The second path which leads up to an understanding of the chemotherapy of virus diseases began in 1922 when a phenomenon was brought to light by Browning and Gulbransen (1922).

It was found that when mice are fed with parafochsin and are subsequently inoculated with a strain of trypanosome resistant to parafochsin, the therapeutic action of trypaflavin is greatly reduced. Schnitzer (1926) showed that to demonstrate this "therapeutic interference" it was unnecessary to use trypanosomes made resistant to parafochsin. Schnitzer and Rosenberg (1926, 1927) and Schnitzer and Silberstein (1926, 1927) further showed that parafochsin would interfere with the chemotherapeutic action of trypaflavin, arsacetin, arspenamine and tartar emetic, whilst pyoktanin (a mixture of penta- and hexa-methyltri-amino-triphenylmethane hydrochloride) interfered with the action of trypaflavin, arsacetin, arspenamine and tartar emetic but not with trypanosan. Other examples of therapeutic interference have been found with yeasts (Wright and Hirschfelder, 1930). A full bibliography is given by Findlay (1939).

These observations, which had their genesis in the cell receptor theory of

Ehrlich, were strangely neglected by biochemists, despite the fact that the possibility of the receptor being a sulphhydryl group was postulated by Schnitzer and Silberstein (1927). In 1927 Quastel and Wooldridge showed that malonate interfered with the action of succinic dehydrogenase, and later, Clark (1937) believed that drugs acted as biological competitors for receptor groups, an example being the competition between oxygen and carbon monoxide for the hæmoglobin molecule. The idea of biological competition, however, received its present form from Fildes (1940) who postulated that chemotherapeutic drugs act as competitors with essential metabolites for specific cell enzymes: to produce a chemotherapeutic remedy it would be necessary so to modify the structure of an essential metabolite that it could no longer function as such but could still compete for the service of the specific enzyme. The classical example of this competition is that between sulphanilamide and *p*-aminobenzoic acid which, it is postulated, is an essential growth factor for organisms susceptible to sulphanilamide (Woods, 1940). That the inhibitory action of *p*-aminobenzoic acid on sulphonamides is an example of biological competition or interference cannot be doubted, but that *p*-aminobenzoic acid is an essential metabolite for most pathogenic bacteria is still uncertain (Sevag, 1946). Apart from the competitive inhibition by *p*-aminobenzoic acid of sulphonamide action on the psittacosis-lymphogranuloma viruses no success has yet been obtained in specifically inhibiting essential virus metabolites of which actually little is known. McKinstry and Reading (1944) examined without result the effect of synthetic pyrimidines on the course of experimental poliomyelitis in the mouse in the hope that compounds of this type might compete with the normal pyrimidine components of the virus for the synthetically active enzymes. The action of acridines, and particularly "phosphine GRN", in inhibiting the multiplication of a coli-bacteriophage were found by Fitzgerald and Babbitt (1946) and Fitzgerald and Lee (1946) to be counteracted by ribonucleic acid, possibly because the acridines compete for some substance related to nucleic acid.

The final path which may lead to an understanding of virus chemotherapy comes from the observations of Hirst (1942 a, b) that certain viruses such as influenza A and B agglutinate the red cells of the chick embryo. This agglutination is specifically inhibited by immune serum, whilst non-specific inhibition is caused by normal sera, normal allantoic fluid and extracts of animal tissues. Hæmagglutination is due to the presence on the red cells of a receptor substance: the influenza virus in causing agglutination acts like an enzyme which attacks a specific substrate in the red cell. The specific substrate is destroyed by periodate and is therefore probably a carbohydrate. It is thus of interest that Green and Woolley (1947) have found that certain complex carbohydrates, apple pectin, citrus pectin, blood group A substance, gum acacia and flax seed mucilage inhibit virus agglutination. Nitroacridine 3582 has no effect on hæmagglutination although it partially inhibits growth of the virus. Apple pectin, on the other hand,

inhibits hæmagglutination and also the multiplication of the influenza virus. This then is an example of biological competition between apple pectin and the receptor substance of the chicken red cell for the influenza virus. It may well lead to the successful chemotherapy of virus diseases before the virus actually penetrates the cell, especially as Horsfall and McCarty (1947) have found that polysaccharides of bacterial origin, as well as from other sources, are capable of modifying the course of infection by the pneumonitis virus of mice.

TABLE I
INTERFERENCE BETWEEN ANIMAL VIRUSES

VIRUS INHIBITED	INTERFERING VIRUS	REFERENCE
	ANTIGENICALLY RELATED VIRUSES (a) Interference <i>in vivo</i>	
Herpes simplex (encephalitogenic strain)	Herpes simplex (non-encephalitogenic strain)	Magrassi (1935).
Yellow fever (viscerotropic strain)	Yellow fever (neurotropic strain)	Hoskins (1935), Findlay and MacCallum (1937).
Rinderpest	Rinderpest (goat-adapted strain)	Pfaff (1938).
Dog distemper	Dog distemper (ferret-adapted strain)	Green and Stulberg (1946), Green (1946).
	(b) Interference in tissue culture	
Poliomyelitis (simian strain)	Poliomyelitis (mouse adapted strain)	Jungeblut and Sanders (1940).
Influenza A (pneumotropic mouse strain)	Influenza A (neurotropic mouse strain)	Andrewes (1942).
Influenza A	Influenza A (inactivated by ultra-violet light)	Henle and Henle (1943, 1944).
Influenza B	Influenza B (inactivated by ultra-violet light)	Henle and Henle (1943, 1944).
Ectromelia	Ectromelia (inactivated by ultra-violet light)	Andrewes and Elford (1947).
Influenza A	West Nile virus	Lenette and Koprowski (1946).
Influenza A	Yellow fever (17 DD high strain)	Lenette and Koprowski (1946).
	ANTIGENICALLY DISTINCT VIRUSES	
	(a) Interference <i>in vivo</i>	
Yellow fever (viscerotropic strain)	Rift Valley fever	Findlay and MacCallum (1937).
Rift Valley fever	Yellow fever (neurotropic strain)	Findlay and MacCallum (1937), De Assumpcao (1944).
Shope fibroma	Virus III	Andrewes (1940).
Poliomyelitis (simian strain)	Lymphocytic choriomeningitis	Dalldorf, <i>et al.</i> (1938, 1939).
Western equine encephalomyelitis	Theiler's mouse virus	Schlesinger, <i>et al.</i> (1943).
Eastern equine encephalomyelitis	Western equine encephalomyelitis	Schlesinger, <i>et al.</i> (1943, 1944).
Vesicular stomatitis	Western equine encephalomyelitis	Schlesinger, <i>et al.</i> (1943, 1944).
Ectromelia of mice	Vaccinia	Andrewes and Elford (1947).
	(b) Interference in tissue culture or in the chick embryo	
Influenza A	Influenza B	Ziegler, <i>et al.</i> (1944 a and b).
Influenza B	Influenza A	
Influenza A	Swine influenza	Ziegler, <i>et al.</i> (1944 a and b).
Swine influenza	Influenza A	Ziegler, <i>et al.</i> (1944 a and b).
Swine influenza	Influenza B	Ziegler, <i>et al.</i> (1944 a and b).
Influenza B	Swine influenza	Ziegler, <i>et al.</i> (1944 a and b).
West Nile virus	Yellow fever (17 DD high strain)	Lenette and Koprowski (1946).
Equine encephalomyelitis (Venezuelan strain)	Yellow fever (17 DD high strain)	Lenette and Koprowski (1946).
Equine encephalomyelitis (Venezuelan strain)	West Nile virus	Lenette and Koprowski (1946).

Owing to the limitation of space it has not been possible to publish the references to this article. They are, however, obtainable on application to the Editor.

VIRUSES AND CANCER

By W. E. GYE, M.D., F.R.C.P., F.R.S.

Director, Imperial Cancer Research Fund.

It is often said, and with apparent justification, that the trouble with cancer is not that we do not know the cause of the disease but that we know too many causes. For example, if coal tar is dabbed repeatedly at any site on the skin of an appropriate animal, for instance the mouse, an epithelioma will arise at that site: tar then is the cause of the induced cancer. Epithelioma of the skin is an industrial hazard among men who work with coal tar. Coal tar is an exceedingly variable mixture of chemical compounds, one of which has been identified as 3:4-benzpyrene, a hydrocarbon of complex structure. This substance, recrystallized until perfectly pure, is capable of acting as a cause of cancer—in laboratory jargon, as a carcinogenic substance—with much greater violence than coal tar. It is a substance now used in laboratories all over the world in studies of the early development of cancers. When it is dissolved in an innocuous oil, sesame oil for instance, and the solution injected under the skin, a cancer of the subcutaneous tissues, a carcinoma, is induced. So far as these tumours are concerned there can be no doubt left in the mind of the experimentalist that benzpyrene is “the cause” of these tumours.

But benzpyrene is only one of several hundred pure chemical substances which are capable of causing cancer. Some are exceedingly active, e.g. methylcholanthrene; some only slightly active and needing prolonged application before a tumour appears. There is no common chemical structure between them. Some are simple substances, such as carbon tetrachloride and even chloroform; some are of such a degree of complexity as to excite enthusiasm in the breast of the pure chemist. Many of the compounds are administered by mouth, the most remarkable instance of this type of substance being aminoacetylfluorene. This compound was discovered in the United States in the course of a search for insecticides. Administered by mouth it is capable of starting cancer in many sites: in the skin, and especially in the external ear, in the breast, the small and large intestines, in the urinary bladder, in the pituitary gland, the liver and elsewhere. Many dyestuffs, the best known of all being butter yellow, are used to initiate cancers of the liver.

It can truly be said that we know some hundreds of chemical substances which are all causes of cancer. But what would the unfortunate victim of X-ray dermatitis and epithelioma say to this? Clearly, that it is abstractly very interesting but that X-rays are also the cause of cancer, and so far as he is concerned, *the* cause of cancer. Likewise the patient with bilharzia infestation and bladder cancer would refer to the action of gross parasites as a cause of cancer. All these ways of starting cancer have been studied in

laboratories and all have been proved valid. There are indeed many ways of starting a cancer, by chemical or physical means or by allowing certain gross parasites to invade tissues, and all are causes in one restricted sense: they act on the tissues with which they are in contact and start, in a way still unknown, a malignant tumour and then are no longer necessary for the continuance of the cancer.

This point deserves closer consideration. Let us suppose that a cancer, epithelial or connective tissue in origin, has been induced by the application of benzpyrene or any other chemical substance. The tumour thus induced has all the pathological qualities of cancer in man, but being in a mouse the opportunity for experimental study presents itself. A small fragment of the tumour is excised aseptically and small pieces, each about 0.02 gm., are placed under the skin of a number of mice. If the mouse with the chemical tumour and the mice to be inoculated are so closely inbred that there is no resistance by the host to the implanted tumour fragment, the grafts grow in every mouse and form daughter tumours. It has been proved as clearly as histology can ever prove anything, that the daughter tumours are derived entirely from the implanted malignant cells and not at all by infection of the host cells. The host mouse acts merely as the host, feeding and caring for the introduced cancer cells. If the injected mice are not inbred and there is an antigenic difference between grafted tissue and mouse recipients, sometimes none of the grafts grow, usually only a small percentage. The process of grafting in this way can be carried on indefinitely and it does not matter whether the original remote cause be a chemical substance or a physical agent like X-rays or a gross parasite like *Tænia crassicolis*. The remote chemical or physical agent is no longer necessary to the continuance of the new growth. The cancer has a life of its own; it lives for and by itself. It is agreed among all competent students that the continuing cause is intracellular and it is this continuing or intracellular cause of cancer which is the central, apparently mysterious, problem of the disease. There is no dispute about the remote provocative causes which have been studied with such intensity during the past twenty-five years; there is much dispute, even passion and anger, about the continuing cause.

RESULTS OF RESEARCH

Cancer is a disease of cells; transformation of neighbouring normal cells into malignant cells rarely, if ever, occurs (the proved exception to this rule will be referred to later); and cancers grow from their own resources. Furthermore, it was quickly demonstrated that cancer is not confined to human beings but is common in domesticated and in wild animals. Its age distribution is the same for men and animals and consequently it is not commonly seen in animals which are killed young for food. But here it is especially important to refer to the fact that in spite of careful work in all countries it was not possible to demonstrate any bacterial cause. Indeed,

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the tumour multiply and can be recovered again and again and used to start more and more tumours. The question was at once posed: is the tumour a true neoplasm? Rous and his assistants investigated the growth, compared its properties with tumours of men and animals, and reached the conclusion that if it is not a true neoplasm then we must find new criteria by which to judge the nature of a new growth. To-day it is universally agreed that the "Rous sarcoma" is a true new growth and that its cause is a virus.

Two hundred or more filtrable tumours of fowls have now been described. They vary in structure and rate of growth and in sites of metastasis formation. The tumour which is universally known as the "Rous sarcoma"—actually the first but only one of more than forty that were studied by him—and the spindle cell sarcoma described by Fujinami in Japan grow rapidly and kill a hen in two to four weeks; a fibrosarcoma described by Begg grows so slowly that usually a chicken lives twelve months carrying the tumour. Other tumours are of endothelium, or muscle or bone. No avian filtrable epithelial tumour has so far been described. All the tumours have their own special peculiarities. Thus the Rous sarcoma metastasizes to the liver, heart and lungs; another tumour described by Rous forms secondary growths in muscle. Begg's endothelioma forms deposits in liver, spleen and in the remnants of the thymus gland in the neck. All have one feature in common, namely, that they are transmissible, some fairly regularly others occasionally, with cell-free filtrates and dried tissues.

But it might be argued that these tumours all occur in the domestic fowl and, since tumours of small mammals are not transmissible with cell-free filtrates, the filtrable tumours of birds merely constitute a disease resembling cancer but not cancer proper. This argument was made untenable by Shope's discovery of a filtrable papilloma of the wild rabbit. The causative virus of Shope's tumour infects the skin epithelium of the domestic rabbit, giving rise to a fleshy papillomatous growth which almost invariably passes into a malignant invasive squamous epithelioma.

During the past ten years, work of the greatest importance has been carried out in the United States on mammary cancer in mice. Most of the work on cancer which led to the fixed belief that the cancer cell is a mutant of a normal cell, or alternatively that the cancer cell owes its powers of unlimited growth and division to a morphological change, was done with mouse mammary cancers. It could be said with justification that of all known tumours the adeno-carcinoma of the mouse mamma is the least likely to yield evidence of a virus etiology. Yet this has now been proved.

The hereditary factor.—In 1911, J. A. Murray proved that mice with a cancerous heredity (in mothers and grandmothers) were three times more likely to develop breast cancer than mice without cancer heredity (*The Fourth Scientific Report of the Imperial Cancer Research Fund*). The work was carried further in America. Pure line strains of mice were bred by brother-sister matings in which as many as 90 per cent. of the females

since it was proved that for successful transmission of a tumour from animal to animal it was essential to implant living cells under the skin, and since it was shown that the tumour which developed at the site where the living cells were placed—the daughter tumour—is formed by growth and division of the living cells of the inoculum, it is not surprising that all the pioneers of cancer research repudiated even the possibility of a microbic—using the word in its widest sense—origin of cancer. Moreover, since the microbic theory of disease appears to be indissolubly associated with the notion of contagiousness of disease, and since no evidence of contagious spread of cancer from person to person, or even within the body by spread from one cell to another, has been found, the case against microbic causation appeared to be absolute.

All these findings in the earliest investigations of cancer were verified again and again in every laboratory engaged in cancer research. As a consequence of these results opinion swung away from the possibility of “infection” in cancer, and this includes virus infection, so strongly that when in 1911 a tumour was discovered which was proved to be caused by a virus the discovery was not accepted as a contribution to the knowledge of cancer. The tumour was regarded as an example of a peculiar disease with some resemblance to cancer—a disease *sui generis*.

THE CONTINUING CAUSE OF CANCER

The pioneers of experimental investigation were very clear in their minds of the distinction between remote causes of cancer, such as tar, heat and X-rays, and the continuing or intracellular cause. The continuing cause excited their attention and consequently the discovery of carcinogenic compounds was delayed for many years. But no progress was made in the intense studies directed towards the discovery of the fundamental essential cause of malignancy. The most favoured explanation was, and still is in some laboratories, that the cancer cell is a variant or mutant of the normal cell. This is clearly a verbal explanation; it is the equivalent of saying that a cancer cell is a cancer cell because it is so. Meticulous study of cells, counting of chromosomes, examining of cytoplasmic structures, measurements of ratios of nuclear volume to total cell volume, and similar studies have all been carried out with the greatest care in the hope of finding some constant material or structural basis for the fundamental properties of the cancer cell, and all have failed.

The rôle of the virus.—In 1911 Peyton Rous discovered that a spindle cell sarcoma of the domestic hen was transmissible by injection of cell-free filtrates. The tumours which formed ten to fourteen days after injection of the filtrate grew rapidly and from them a filtrate could be prepared, and with such small amounts as one-tenth of a cubic centimetre other tumours could be started in normal chickens. The significance of this discovery is self-evident. The agent which causes the tumour multiplies as the cells of

the tumour multiply and can be recovered again and again and used to start more and more tumours. The question was at once posed: is the tumour a true neoplasm? Rous and his assistants investigated the growth, compared its properties with tumours of men and animals, and reached the conclusion that if it is not a true neoplasm then we must find new criteria by which to judge the nature of a new growth. To-day it is universally agreed that the "Rous sarcoma" is a true new growth and that its cause is a virus.

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developed mammary cancer. Other inbred strains were obtained in which no cases occurred. We now possess a number of such "high" and "low" cancer lines. Little, Strong, Bittner and others showed that when a female of a high cancer line was mated with a male of a low cancer line, the females of the hybrids gave a high percentage of mammary cancer; in the reverse experiment in which a male of a high cancer line is mated with a female of a low cancer line the female progeny do not develop cancer. The tendency to cancer thus appeared to be carried only by females and so far as the genetics of the process is concerned Mendelian principles appeared not to apply. At first the inheritance was described as an extra-chromosomal influence. Later it was discovered by Bittner that the occurrence of mammary cancer depends upon the transmission by mother's milk of a virus. The virus can be found in the blood and tissues of a mouse which has been fostered by a mother of a high cancer line. Without the virus no tumour develops and the tumour which has been initiated by virus is the richest known source of further supplies of virus. All the evidence points to the conclusion that the "milk factor", which is now regarded by workers in this field as a virus, multiplies as the cancer cells multiply.

There are other examples of virus tumours. Lucké in America has described an adeno-carcinoma of the kidney of frogs which is caused by virus; that is to say, a tumour in which it is possible to demonstrate a virus as a continuing cause. A virus papilloma of the lip and tongue of the domestic rabbit has also been described, but the most important piece of evidence that a virus may play a part in cancerous growths was discovered forty years ago simultaneously in Ehrlich's laboratory in Frankfort and in the laboratories of the Imperial Cancer Research Fund, namely, the acquisition of malignant properties by connective tissues which form the stroma of certain mammary cancers of mice. Briefly stated, it was found that when a spontaneous cancer of the breast was grafted in other mice a sarcoma formed in the supporting stroma of the daughter tumour. The possibility that a virus passes from malignant epithelial cell to normal connective tissue cell is, and was to the discoverers, evident; but the probable significance of the observation was drowned in an ocean of words devoted to histological description and controversy. Ehrlich and Bashford had only stock mice of mixed ancestry as experimental animals and in these mice the phenomenon is rare: to-day most laboratories have highly inbred high cancer lines available, and it has been found that in such mice sarcoma formation in the stroma is very common.

CONCLUSION

Although not all the evidence of virus activities in cancer has been described, it is right to conclude with the statement that there is much evidence that viruses act as the continuing cause of cancer and that there is no factual basis for any other explanation.

SOME VIRUS DISEASES IN DOMESTIC ANIMALS

By G. F. BODDIE, B.Sc., M.R.C.V.S., F.R.S.E.

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SOME of the most troublesome of the epidemic diseases affecting domesticated animals are those caused by viruses. As in all these diseases the reservoir of infection is the living infected animal, the destruction of all infected animals in a self-contained community will dispose of the source of infection. This method was used in dealing with rinderpest (cattle plague) and sheep-pox in Great Britain and, since the introduction of further infection can be prevented, it has been possible to maintain these islands free from these diseases. The same method is used in dealing with foot and mouth disease, but owing to repeated introduction of infection outbreaks of the disease continue to occur. Although many of the virus diseases of animals are transmitted by contact between infected and susceptible animals, infection may be transferred by mediate contagion; this takes place in foot and mouth disease and also in swine fever. Rabies (hydrophobia of man) is peculiar in its mode of transmission in that infection is acquired by inoculation, the most common method being the inoculation of the virus by the bite of a rabid dog. Louping ill, a disease affecting a number of species but principally a disease of sheep, has an almost unique manner of spread in that the virus is transferred by the bite of an infected tick.

The viruses show marked selectivity for particular tissues; thus cow-pox produces characteristic skin lesions, louping ill and rabies are manifested by nervous signs, and foot and mouth disease gives rise to lesions on the feet and in the mouth.

An important feature of many virus diseases is the high degree of infectivity. Fortunately a solid immunity can be acquired against some of these viruses, either by the animal passing through a natural attack of the disease or by artificial immunity created by the inoculation of avirulent virus. Unfortunately in some cases there are several strains of the causal virus and these are not similar antigenically, so that immunity against one strain does not protect an animal against the other strains. It is noticeable that where a disease is indigenous to a country the native animals possess a partial immunity and if they contract the disease it pursues a mild course; but should imported animals come in contact with the virus or should the virus be imported into a country free from infection, the disease appears in a severe and malignant form. Rinderpest in African and Asiatic cattle may run a relatively benign course, but if introduced amongst European cattle runs a very severe course. Sheep-pox in the Balkans is quite a mild disease, but its accidental appearance in Northern European countries has been calamitous.

FOOT AND MOUTH DISEASE

Foot and mouth disease affects cloven-hoofed animals. The horse is not susceptible. Cases in human beings have been reported, but unless the presence of the virus was demonstrated biologically the diagnosis cannot be accepted as being adequately confirmed. All the available evidence is that in human beings susceptibility must be very low indeed.

Three main strains of virus are recognized and there is no cross immunity between these strains. It is suggested that there may be numerous variants of these main strains. Recent work has shown that the hedgehog is susceptible and this animal may play a part in the spread of infection.

The virus of foot and mouth disease has remarkable powers of survival away from the living animal body, especially if dry. Chilling or freezing of the virus maintains its virulence for very long periods. In some of the South American countries, from which Great Britain imports meat, foot and mouth disease is endemic. Although a system of inspection exists, it is impossible to detect animals in the incubative stage of the disease; the virus of the disease is present in the tissues of such animals and is preserved by chilling or freezing in transit. Should the remnants of such meat be deposited in food refuse fed to pigs they may acquire an infective dose of virus. In order to obviate this risk all swill should be boiled before it is fed to livestock. The virus has been introduced into this country by contaminated straw that has been used for the packing of imported goods. There is strong circumstantial evidence that infection may have been carried by migrating starlings.

The incubation period varies from two to ten days but in many cases it is found to be between two and three days. The first sign of the disease is a sharp, febrile reaction, and in from one to two days the lesions develop.

In cattle and sheep there is marked discomfort in the mouth, the animals experience difficulty in feeding, and in cattle salivation is profuse. Vesicles develop in the mouth, particularly on the dorsal surface of the tongue; these rupture in a day or two leaving superficial sores. The lesions on the feet cause lameness; vesicles can be seen on the finer skin of the interdigital space and the bulbs of the heels. Separation of the horn takes place around the coronary band and may involve the whole horn so that the complete claw is shed. In pigs, lesions on the feet are the predominant feature of the disease, vesicles on the snout being seen only occasionally.

Except in the malignant form the mortality in adult cattle is very low, seldom exceeding 2 per cent. The disease causes serious loss in bodily condition; the milk yield practically ceases, and pregnant animals may abort. In calves the disease may take the form of a rapidly fatal septicæmia.

Control measures.—In Great Britain the disease is controlled by the destruction of all affected animals and their immediate contacts. The carcasses are cremated, buildings are disinfected, and the movement of cattle, sheep and pigs in the neighbourhood of the infected premises is restricted.

Experimental research has evolved two forms of vaccine. In one, the virus obtained by the filtration of infective material is adsorbed on to aluminium hydroxide and treated with formalin. This vaccine has been used in countries where the disease is endemic, a cordon of vaccinated animals being formed around the nucleus of the outbreak. The vaccine must be prepared from the particular strain of the virus causing the outbreak. Another form of vaccine is prepared by treating with crystal violet the virus in blood from infected animals. This vaccine has been shown to be effective, but one difficulty is the large quantity of infective blood required.

The development of an efficient vaccine would make it possible to control the disease in those countries where the endemic character of the disease renders impossible eradication by the slaughter policy.

RINDERPEST

Rinderpest or cattle plague is an acute disease of cattle; other ruminants may contract the disease but in them it usually assumes a mild form. Rinderpest is prevalent in Asia and Africa, although the Union of South Africa has been freed from the disease. The virus does not appear to survive more than two days away from the living animal. Indigenous cattle in affected countries tend to develop the disease in a mild form with a relatively low mortality, but in European cattle the disease is usually severe in character and the mortality may exceed 90 per cent. Rinderpest is characterized by acute inflammation of the mucous membranes, the most marked lesions being found in the alimentary tract, where ulceration occurs. At one time prevalent in this country the disease was eradicated by the slaughter policy, the re-introduction of infection being prevented by the prohibition of the importation of ruminants from countries where the disease is endemic.

In India, vaccination of cattle with attenuated virus has given some success. The method of attenuation is the passage of the virus through goats until the pathogenicity for cattle has been reduced. This method has not proved successful in Africa, where the susceptibility of the cattle is too high to permit the use of goat-attenuated virus. A vaccine has been prepared by the treatment with formalin of virus grown by tissue culture.

COW-POX AND SHEEP-POX

Historically, *cow-pox* is of interest because of Jenner's observation of the cross immunity existing between smallpox and cow-pox. Outbreaks of cow-pox occur from time to time in this country. Cow-pox is, as a rule, a benign local condition affecting principally the udder and teats of milking cows. The presence of the lesions on the teats interferes with milking, and of course the milk from an affected cow is not fit for human consumption.

There have been no outbreaks of *sheep-pox* in Great Britain since the middle of the nineteenth century. The disease is still prevalent in the Balkans and along the shores of the Eastern Mediterranean. In countries where the disease is endemic it runs a mild course with very slight general reaction and the development of the typical variolous lesions on those portions of the skin not covered by the fleece. If introduced among susceptible sheep, the disease assumes a severe form causing a high proportion of cases of rapidly fatal septicaemia.

LOUPING ILL

Louping ill, although principally a disease of sheep and cattle, has been reported in horses and pigs. The disease may occur in human beings who

have been bitten by infected ticks and also in laboratory workers whose nasal mucous membranes have been infected by the virus. The virus of louping ill is transmitted by the bite of the tick, *Ixodes ricinus*, but does not pass through the egg of the tick. Larvæ and nymphs acquire infection when feeding on an infected animal and spread infection when feeding as nymphs and adults. The seasonal incidence of the disease coincides with the periods of activity of the ticks.

Experimentally, it has been shown that from eight to eighteen days after artificial infection a sharp febrile reaction takes place during which the virus is present in the blood stream. This stage is not accompanied by any well-defined symptoms and in field conditions usually passes unnoticed. After an interval of about three weeks a second febrile reaction takes place, and this coincides with the invasion by the virus of the central nervous system and is characterized by the development of the nervous symptoms. The nervous lesions are those of an encephalomyelitis.

The clinical manifestation of the nervous lesions are muscular tremors—hence the colloquial name “trembling”; incoordination of gait causing the animal to progress by a series of leaps—so the designation “louping ill”. Subsequently, paralysis of both fore and hind limbs develops.

Control measures.—Although the intensity of the incidence of the disease may be limited by measures taken to control the tick population, such measures are of restricted value. Many animals acquire an immunity through receiving sublethal doses of the virus by tick bite. Artificial immunity can be created by a vaccine prepared by treating with formalin the brain and spinal cord of artificially affected sheep. This vaccine gives a satisfactory immunity in cattle and sheep. It is, however, not suitable for use in lambs. Lambs acquire passive resistance from their immune mothers; this resistance persists for about twelve weeks; lambs possessing passive immunity do not respond to the stimulus of vaccination. Vaccine prepared from virus grown on tissue culture has not proved so successful as that prepared from animal tissues.

CANINE DISTEMPER

Distemper in dogs is world-wide in distribution; the disease is constantly present in any area where there is a substantial canine population. In smaller canine communities the disease may die out when following an epidemic all the susceptible animals have contracted the disease. In larger canine communities, although the disease is constantly present, the incidence varies, periods of increased incidence occurring at fairly regular intervals. The virus of canine distemper was first isolated by Carré of Alfort; his observations were repeated by Lignière and subsequently confirmed by Laidlaw and Dunkin. The virus of canine distemper is not pathogenic to cats. The incubation period following experimental infection is four days; under field conditions it does not exceed seven days. The virus is present in the blood stream and secretions from mucous membranes in the early stages of the disease, but has largely disappeared by the time secondary invading organisms have become active.

The typical case of canine distemper is characterized by fever and catarrh of the mucous membranes. Many of the complications of distemper are due to the activities of secondary invaders, the patchy broncho-pneumonia being associated with *B. bronchisepticus* and the gastro-enteritis with streptococci and coliform organisms. In some respects, the most troublesome of the complications of distemper are those involving the nervous system. These are due to the action of the virus on the central nervous system, and take the form of epileptiform convulsions, chorea and paraplegia.

Immunization.—In the early stages of the disease, before the secondary organisms have come into play, homologous anti-distemper serum is used in the treatment of the disease. If successful, treatment with serum cuts short the illness due to the virus and the mucous membranes are not invaded by the secondary organisms. Unfortunately, anti-distemper serum is not so successful in preventing the development of nervous complications; although the initial illness be curtailed, signs of nervous damage may appear about three weeks later. Distemper is so prevalent that the majority of dogs, unless kept in conditions of strict isolation, will encounter infection before they are a year old. Puppies born of immune mothers apparently acquire an effective immunity from the mother, but this is only a passive immunity which has waned by the time the puppy is six weeks old. Anti-distemper serum conveys a passive immunity against infection that is adequate for about seven days: unless reinforced by a further injection of serum this immunity fades, and has probably largely disappeared by the fourteenth day after injection. There are three methods employed in the active immunization of dogs against distemper:—

(1) *The vaccine-virus method*, in which a vaccine consisting of formalinized virus is injected, followed fourteen days later by injection of living virus. Under favourable conditions the vaccine produces sufficient immunity for the animal to withstand the living virus, which enhances and stabilizes the immunity produced by the vaccine. It is essential that the animal should be free from infection at the time the process of immunization is begun and that it should not be exposed to infection during the period of immunization. When young animals can be kept under conditions of isolation, these desiderata may be fulfilled, but under ordinary conditions it is difficult if not impossible to fulfil them.

(2) *In the virus-serum method*, living virus is injected into the animal and its action is controlled by the administration of anti-distemper serum. The success of this method depends upon a fine balance between virus and serum so that the virus is able to stimulate active immunity without causing the disease. Should the virus be preponderant, the probability is that distemper will be caused; should the serum be preponderant, active immunity will not result. The necessary balance between virus and serum has been achieved and in the majority of dogs this method of immunization has proved satisfactory. There is a proportion of dogs that are found not to be

suitable subjects for this process of immunization; some are unusually susceptible to infection and contract distemper, others do not develop an effective immunity.

(3) In America, a method of immunization of dogs against distemper has been based on the principle that virus passed through successive generations of ferrets loses its pathogenic properties for dogs but still remains antigenically active. Virus that has been passed through over fifty generations of ferrets is used in this method, and it is claimed that the method is safe and effective.

FELINE DISTEMPER

The term feline distemper has been used to describe more than one independent clinical entity. Contagious feline catarrh is a highly infectious form of catarrh affecting all the mucous membranes. The etiology is not known but there is some epidemiological evidence suggesting that it may be due to a virus and that carrier cats perpetuate the infection.

It has been shown that contagious feline enteritis is caused by a virus. The mortality rate due to this disease is over 60 per cent. and the illness runs a very short course. The lesions of the disease are practically confined to the intestine, in some cases to a relatively restricted area in the ileum. Many cats die in a few hours without showing any sign of diarrhoea but those that survive longer develop profuse diarrhoea that may be blood-tinged. An interesting feature of this disease is the change in the blood picture, the white cell count dropping from 17.2 ± 6.6 thousand to as low as 1000. Experimentally, artificial immunity has been created by the use of a vaccine prepared by the action of formalin on the causal virus.

RABIES

The relationship between rabies (or hydrophobia) in man and the bite of a rabid animal has been recognized for centuries. Pasteur in 1881 was able to prove that the infective agent was present in the central nervous system; in 1903, Remlinger proved that the disease was caused by a filtrable virus, and Negri described the cell inclusions known as Negri bodies. The disease is widely distributed throughout the world, though Australia has remained free. Although various wild mammals do in certain countries play a part in transmitting the disease, the dog is the most important. Infection can only be acquired by inoculation and usually results from the bite of a rabid dog.

In the dog, rabies assumes two forms, the furious form in which the dog is aggressive and attacks anything in its path, and the dumb form in which the dog, although apparently virtually paralysed, is still able to bite if provoked. In the furious form dogs go off on the run and may travel many miles, infecting victims they meet on their travels. A rabid dog that escaped from Plymouth ended its career in South Wales.

Preventive measures.—In order to prevent the re-introduction of rabies

infection into Great Britain all imported dogs are placed in quarantine for six months. From time to time dogs in quarantine develop rabies. It is important to realize that one such case occurring out of quarantine would, in all probability, lead to another outbreak with the possibility of human cases occurring. In those countries where rabies is endemic dogs are inoculated by Pasteur's method or a modification of it. The inoculation of dogs in Great Britain is not permitted and the fact that a dog has been inoculated does not exempt it from the quarantine regulations. The disease, if symptoms appear, is almost invariably fatal. Diagnosis of rabies in affected animals is based on the history and clinical signs, confirmation depending upon the demonstration of Negri bodies in the cells of the hippocampus and biological demonstration of the virus in tissues from the suspected animal.

SWINE FEVER

In its uncomplicated form, swine fever is essentially a virus septicæmia. The disease is both highly contagious and fatal. In acute cases the post-mortem lesions are those of a septicæmia. In less acute cases the most characteristic lesions are the ulcers that form in the intestine, especially in the region of the ileo-cæcal valve. Owing to proliferation of tissue the ulcer tends to stand up above the level of the surrounding mucous membrane and the heaped-up appearance of the ulcer is very noticeable. Diagnosis of any disease in the living pig is attended with difficulty, and in swine fever there is a good example of a diagnosis that must be based on the epidemiology, clinical signs and lesions.

Individual outbreaks of swine fever are best dealt with by slaughtering all the pigs on the farm. Methods of producing passive immunity against swine fever have proved unsatisfactory. Methods of producing active immunity with virus serum, though they proved successful in America, did not succeed in Great Britain. A crystal-violet vaccine is now being used extensively in both America and Great Britain; an effective immunity lasting for at least six months is produced.

FOWL-POX

There are three main forms of the disease fowl-pox. In the skin form, warty growths appear on the comb, wattles, and at the commissures of the mouth and eyes. In the mouth form, yellowish necrotic material is found attached to the tongue or to the larynx; this form has been termed the diphtheritic type. In the oculo-motor form the infra-orbital sinuses become infected and swollen, displacing the eye and tending to close it. The nasal chamber and palatine cleft are frequently blocked with yellowish caseous material.

An efficient *immunity* against fowl-pox can be created by the application of living pigeon-pox virus to the scarified skin of the hen's thigh. Chickens upwards of six weeks can be vaccinated by this method. No general reaction occurs and in particular egg production receives no check.

THE MEANING AND MEASUREMENT OF PAIN

By LORD MORAN, M.C., M.D.

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PAIN is a common symptom, but what is known about it has not passed into general circulation. The modern physician is apt to substitute a box of tricks, his own particular technical apparatus, for a thought-out analysis of the evidence, although he must know that in the practice of his art it is only his wisdom in the interpretation of symptoms which lifts him above his fellows; and of these symptoms the most significant is pain. Contemporary physiology, for its part, has been more concerned, as Professor Adrian confesses, with the details of the nervous mechanism responsible for pain than with its biological functions. Yet if this mechanism is to attract the attention of the body of the profession, the meaning, the motive of pain must be plain, within the limits of our knowledge.

THE DISTINCTION BETWEEN SUPERFICIAL AND DEEP PAIN

The first thing necessary to know about pain is where it arises, what organ is at fault. When dealing with pain arising in a superficial structure, by which I mean the skin or the second sensitive layer, which consists of the deep fascia encasing the limbs and trunk and any periosteum, ligament or tendon that is subcutaneous, no difficulty arises. Pain originating in any of these structures is accurately located. A prick on the skin of the finger is felt exactly at the site where it has been pricked. But pain arising from a deep structure is felt at a distance from the point stimulated. For example, in a subphrenic abscess the pain is referred to the point of the right shoulder, and in angina pectoris the pain may be felt in the left arm. Superficial and deep pain are quite distinct sensations; indeed the contrast between skin pain and pain arising from any structure deep to the skin is such that Lewis was reluctant to include both under the term pain. Skin pain is associated with brisk movements, a quick pulse, and a sense of invigoration, whereas deep pain, which is so diffuse and so inaccurately localized, is found with a slow pulse, quiescence, nausea, sweating, and sometimes with local rigidity of the muscles of the abdominal wall accompanied by tenderness. Nausea is part of the deep-pain syndrome, which is in consequence sometimes labelled "sickening" pain. Nausea never occurs with superficial pain; it is only found when deep structures are affected, and in particular in visceral pain—angina, and gall-stone, renal and intestinal colic.

Why is skin pain so accurately and deep pain so inaccurately localized? If the periosteum of the tibia (a superficial structure) is jabbed by a hypodermic needle, the pain is accurately located, but if the periosteum of a lamina

of a vertebra (a deep structure) is stimulated, the pain may be referred to a remote area. The periosteum in both cases has the same structure. It is therefore the depth at which the tissue lies and not the nature of the tissue itself which determines the accuracy with which pain is located when the tissue is injured. This illustration seems to suggest that precision in locating an injury is found when it has proved serviceable in the history of the species, or, to put it differently, it is a matter of education; the power to locate has been sharpened by past experiences.

THE PURPOSE OF SKIN PAIN

The significance or motive of skin pain is not in doubt. The surface of the body is provided with pain nerve endings so that it furnishes quick and immediate responses to injury. The very anatomy of the naked nerve endings suggests that they were designed to pick up warnings from outside which might come in many different forms. We are familiar with illustrations of the value of skin pain to the individual, such as the quick protective spinal reflex when the arm is withdrawn after it has been burnt by a match. Trotter pointed out that without this provision man would not be able to move freely and with comparative safety in a world so largely stocked with hard and angular objects. Lewis stressed the same point when he affirmed that accurate localization of skin pain is essential to avoid repeated injury by the same agent. How effective pain is as a protective shield is shown when the shield is removed by disease. Charcot's joint, found in tabes, is the cumulative result of minor injuries of which the patient is unaware. If his limb had been sensitive to pain the joint would have been spared; as it is he uses it ruthlessly and adds continually to the original lesion. A simple sensory defect has converted an injury into a progressive, destructive arthritis.

Superficial or skin pain is not a source of error in diagnosis, but I dismiss it here with some reluctance, for Lewis's planned study of skin pain is a beautiful example of work inspired by a knowledge of the experimental method, checked and guided by clinical experience. The experimental method of pain differentiation is utilized for information which clinical medicine cannot give. Let me be more precise. An observant physician may have noticed that when he has injected cocaine there is a stage at which pain is lost but touch remains intact. But only the experimental method can tell him why this dissociation happens. At a certain stage in the action of cocaine the smaller nerve fibres (which conduct pain) cease to conduct, leaving the larger fibres (which conduct touch) still in action. As a consequence, at this stage pain is lost but touch remains intact.

ERYTHRALGIA: CAUSALGIA: HERPES ZOSTER

In seeking the motive of pain, it is significant to find the same response to injury in conditions which at first sight seem to have little in common. If

the white forearm is exposed to sun the skin is injured, and we say that the red and tender skin has become hyperalgesic. Chemical substances are produced as the result of the skin injury which act on the pain nerve endings and make them unduly sensitive. Needle pricks, too light to cause pain elsewhere in the skin, are now painful where the skin is hyperalgesic; the friction of clothing causes pain, and a slight rise of temperature, such as the warmth of bed, hurts. This state of the skin is called *erythralgia*.

Precisely the same train of events occurs in *causalgia*. If a nerve, commonly the median or sciatic, is bruised or partly cut through, within a few days burning pain develops in the territory of the nerve, associated with extreme tenderness. The pain is so easily provoked, and so severe, that the victim shrinks from contacts, guarding apprehensively the injured limb. The tender skin becomes red and purple, glossy, devoid of wrinkles, and often wet with sweat. This is the sequence of events: first, the injury (an irritative nerve lesion); secondly, the injury gives rise to centrifugal nerve impulses, leading to the release of substances in the skin. These substances cause the erythralgic skin.

In *herpes zoster* the mechanism is fundamentally similar to that of *causalgia*. When the posterior root ganglion is injured in herpes, or when the median or sciatic nerve is bruised in *causalgia*, centrifugal nerve impulses release substances in the skin which produce the skin lesions of both *causalgia* and *herpes zoster*. To put it differently, the erythralgic skin found in both herpes and *causalgia* is the result of long-continued centrifugal nerve impulses. When the white forearm is exposed to sun the same end-results are found as when the posterior root ganglion is damaged.

Lewis believed that the substance released by direct injury to the skin from exposure to the sun is the same chemical factor which is liberated when centrifugal nerve impulses cause changes in the skin in herpes and *causalgia*. He went further. He thought it probable that there was a common mechanism causing all instances of referred hyperalgesia, not only the hyperalgesia of arthralgia, *causalgia* and herpes, but also the tenderness of the skin of the cheek associated with toothache, the hyperalgesia of the whole territory of the 2nd division of the fifth nerve found in catarrh of the antrum, and the hyperalgesia of the skin of the chest over the left side in angina pectoris.

There is no difficulty in accepting his explanation of the hyperalgesia following direct injury to the skin, but it must be admitted that there is no satisfactory explanation of the tenderness of the skin in angina. Hyperalgesia, which may be defined as pain arising from stimuli that commonly are painless, is a response to injury or to disease. But does it serve a useful purpose in the defence of the individual? It is easy to answer in the affirmative when abdominal tenderness shields an inflamed appendix or gall-bladder, or in the case of a tender whitlow. It is more difficult to explain the hyperalgesia of angina. That hyperalgesia is often serviceable in diagnosis is not in doubt. The distribution of the tenderness at the tip of the shoulder in disease of the gall-bladder is a case in point.

LOCALIZATION OF "DEEP PAIN"

The failure to make full use of existing knowledge of pain is a common source of error in diagnosis; it has its roots in ignorance of the manner in which pain arising in deep structures is not usually felt in them but is referred to the skin. Deep pain may arise from disease of the viscera or from a lesion of a deep somatic structure, such as one of the vertebræ, a muscle or an interspinous ligament. In both visceral and somatic pain, the pain is referred to a segment of the skin. Such a segment is made graphic when inflammation of the ganglion of a particular posterior nerve root gives rise to herpes zoster. Sherrington mapped out these segments systematically on the skin of a monkey by stimulating the posterior nerve roots, one by one. The point I wish to emphasize, the point that is so commonly forgotten, is this: pain arising from any deep structure, whether it be a viscus or a deep somatic structure supplied by the same segment of the cord, will have the same segmental distribution and may be accompanied by the same reflex signs.

Lewis has driven the point home. He injected normal saline into the left eighth cervical or first dorsal interspinous ligament of a man who was familiar with the pain of angina pectoris, and reproduced the essential features of former anginal attacks. I shall borrow another illustration from the same source. Lewis injected with normal saline the first lumbar ligament, and produced signs and symptoms which closely resembled those seen in renal colic; the typical distribution of the pain, the retraction of the testicle, the palpable rigidity and deep tenderness of the lowest part of the abdominal wall of the corresponding side—nothing was wanting.

The pain in renal colic is a good illustration of segmental pain. As the stone descends the ureter it might be expected that the pain would descend with it—but this does not happen. At whatever level the stone may be, the same characteristic segmental pain occurs, the segments in question being L1 and L2. We forget this at our peril.

A woman, in early middle age, complained of pain resembling renal colic, but extensive investigations failed to reveal any abnormality in the urinary tract. At last a physician elicited that the pain had begun when she was recovering from a general anæsthetic in the course of which she had fallen out of bed. This led to an X-ray of the spine, which revealed an old crush fracture of the tenth thoracic vertebra. The error in diagnosis arose through failure to investigate all the possible causes of segmental pain at this particular level.

Visceral lesions as the cause of pain are so common that the possibility that a deep somatic structure may be the source of the trouble is apt to be overlooked. A more common illustration of the same mistake is when sciatica is treated as a local lesion in a patient in whom the pain is due to pressure on the first and second nerve roots by a slipped disc. Once it is recognized that the pain is segmental, the rest is a matter of remembering the structures in that segment which might lead to this pain.

In describing the referred pain from visceral or somatic disease, I mentioned the associated muscular rigidity and tenderness. The rigidity of the abdominal wall covering some diseased viscus is often helpful in diagnosis,

particularly in a diseased appendix or gall-bladder. It is a spinal reflex, probably of a protective character. The sensation of gripping in the chest in angina pectoris may be due to intercostal spasm; the upper intercostal muscles are rigid. Neck rigidity associated with intracranial disease is another illustration of the same process.

THE EXPLANATION OF REFERRED PAIN

Why should pain arising in the heart be referred to the territory of the nerves of the arm? Sturge's original theory was at least a coherent explanation, if it had been capable of proof.

Sturge argued that the same segment of the cord receives afferent impulses from the diseased heart and from the arm. The stream of impulses from the heart irritates this segment of the cord so that afferent impulses reaching it from the arm, which previously did not lead to pain, are now painful owing to the lower threshold. This theory makes referred pain explicable, but it has never been proved and there are some reasons for doubting its validity. Lewis held that it was quite unnecessary to concoct such an elaborate explanation. The bias in favour of surface reference is, he claims, a matter of faulty localization. The sensorium is able to recognize the skin as the source of a particular pain; it is not able to localize the pain from deep structures, so imperfect is their pain innervation, and in default refers them to the nerve endings in the skin of the same segment. The power to localize develops when such power has proved serviceable in the history of the species, namely, the superficial coverings of the body, of which man is, naturally, most conscious.

In brief, all this work on localization of pain comes to this: we may hope to learn the segment or segments in which deep pain is distributed and the side of the body in question. It is something, but it is not enough. Greater accuracy in the interpretation of the significance of deep pain can only be attained by careful consideration of other factors, and in particular of the circumstances in which pain appears.

CIRCUMSTANCES IN WHICH PAIN APPEARS

The pain of gastric ulcer.—Pickering's work on pain in gastric ulcer is an example pat to my purpose. He does not accept the current view that the pain is the result of contraction of the stomach, since he found no change in the intra-gastric pressure and was able to prove by the use of X-rays that localized spasm had no part in the production of the pain. Pickering demonstrated that when the pH of the gastric juice falls below a certain level and the contents of the stomach become more acid, pain occurs.

Taking a clue from clinical experience that pain is relieved by food, by the administration of alkalis, or by vomiting, he sought confirmation of his thesis by the experimental method. He noticed that the pain in a patient with gastric ulcer vanished when the stomach was emptied. When the contents of the stomach were put back by means of a stomach pump, the pain returned. But if the contents were neutralized they could be returned to the stomach without exciting pain. Pickering succeeded in producing gastric pain in a patient with an ulcer by putting acid in the stomach; the pain disappeared on neutralizing the acid. But the introduction of acid into the stomach only led to pain when there was an ulcer in the stomach, and Pickering proved, by taking frequent samples of the stomach contents, that the occurrence of pain bore a direct relationship to the pH. He drew attention to the

value of such knowledge in avoiding errors in diagnosis by an apt illustration:—

A man of middle age complained of pain in the left axillary line at the level of the eighth rib. On examination he was found to have a palpable mass in the upper abdomen. The distribution of the pain was unusual and the diagnosis would have been in doubt, but treatment clarified the issue. The pain was difficult to control by morphine, but it responded at once to milk and alkalis, and its gastric origin was confirmed by laparotomy, which revealed an ulcer with matted adhesions.

Wolff studied the effect of various stimuli applied directly to the mucous membrane of the stomach through a large gastric stoma. Pricking, faradization, acids and alkalis caused no discomfort, but when the gastric mucous membrane was inflamed, congested or ulcerated, these agents provoked pain. It is not known whether these conclusions are valid for the rest of the alimentary tract.

Cardiac pain.—If gripping movements of the fingers are carried out rapidly, after some time a little ache may be noticed in the muscles of the forearm. If before these gripping movements are begun the circulation in the arm is arrested, and kept arrested by the armlet of a sphygmomanometer, the contraction of the flexor muscles of the forearm caused by these gripping movements will lead in about half a minute to a disagreeable pain, which presently becomes intolerable. When the armlet is released so that the circulation is restored, the pain vanishes completely within three seconds. The pain is due to the production of a substance which Lewis calls the P factor; it is irrelevant here to discuss whether this P factor is or is not lactic acid. The P factor is produced when muscles are used and contract under normal conditions, but if the circulation is arrested so that the dispersal of the P factor is prevented, it accumulates until it reaches a level that leads to pain. When there is no obstruction to the blood flow, the P factor either cannot rise to the level necessary to excite pain, or at most it leads to the little ache to which I have referred. Arrest of the circulation alone will not provoke pain; muscular contractions are necessary to produce the P factor; the arrested circulation merely impedes its dispersal so that it accumulates until it causes pain. And this is the explanation of *intermittent claudication*. The muscles contract in the absence of an adequate circulation, and so the P factor accumulates and causes pain.

A relative of mine, a man of fifty-five who was handicapped by mitral stenosis and auricular fibrillation, sent for me early one morning. He complained of intense pain in one leg, which was blanched below the knee. The pain from this embolus persisted for six weeks and he suffered from intermittent claudication for the rest of his days; he died in his eighty-second year. He was at some pains to hide his frailty from his friends; when the pain came on he would pause to look into a shop window; when after a time it had passed, he resumed his walk, but when it returned he displayed renewed interest in the shop window.

Lewis pointed out that the same pain occurred in a man's leg if he were made to walk a hundred yards after the circulation to his leg had been arrested.

In *myocardial ischæmia*, which is the cause of cardiac pain, the same cycle of events is seen. The blood flow to the heart muscle may be decreased

particularly in a diseased appendix or gall-bladder. It is a spinal reflex, probably of a protective character. The sensation of gripping in the chest in angina pectoris may be due to intercostal spasm; the upper intercostal muscles are rigid. Neck rigidity associated with intracranial disease is another illustration of the same process.

THE EXPLANATION OF REFERRED PAIN

Why should pain arising in the heart be referred to the territory of the nerves of the arm? Sturge's original theory was at least a coherent explanation, if it had been capable of proof.

Sturge argued that the same segment of the cord receives afferent impulses from the diseased heart and from the arm. The stream of impulses from the heart irritates this segment of the cord so that afferent impulses reaching it from the arm, which previously did not lead to pain, are now painful owing to the lower threshold. This theory makes referred pain explicable, but it has never been proved and there are some reasons for doubting its validity. Lewis held that it was quite unnecessary to concoct such an elaborate explanation. The bias in favour of surface reference is, he claims, a matter of faulty localization. The sensorium is able to recognize the skin as the source of a particular pain; it is not able to localize the pain from deep structures, so imperfect is their pain innervation, and in default refers them to the nerve endings in the skin of the same segment. The power to localize develops when such power has proved serviceable in the history of the species, namely, the superficial coverings of the body, of which man is, naturally, most conscious.

In brief, all this work on localization of pain comes to this: we may hope to learn the segment or segments in which deep pain is distributed and the side of the body in question. It is something, but it is not enough. Greater accuracy in the interpretation of the significance of deep pain can only be attained by careful consideration of other factors, and in particular of the circumstances in which pain appears.

CIRCUMSTANCES IN WHICH PAIN APPEARS

The pain of gastric ulcer.—Pickering's work on pain in gastric ulcer is an example pat to my purpose. He does not accept the current view that the pain is the result of contraction of the stomach, since he found no change in the intra-gastric pressure and was able to prove by the use of X-rays that localized spasm had no part in the production of the pain. Pickering demonstrated that when the pH of the gastric juice falls below a certain level and the contents of the stomach become more acid, pain occurs.

Taking a clue from clinical experience that pain is relieved by food, by the administration of alkalis, or by vomiting, he sought confirmation of his thesis by the experimental method. He noticed that the pain in a patient with gastric ulcer vanished when the stomach was emptied. When the contents of the stomach were put back by means of a stomach pump, the pain returned. But if the contents were neutralized they could be returned to the stomach without exciting pain. Pickering succeeded in producing gastric pain in a patient with an ulcer by putting acid in the stomach; the pain disappeared on neutralizing the acid. But the introduction of acid into the stomach only led to pain when there was an ulcer in the stomach, and Pickering proved, by taking frequent samples of the stomach contents, that the occurrence of pain bore a direct relationship to the pH. He drew attention to the

due to the first injection is at its height, a second injection of histamine is given, it will banish the headache. This second injection produces vasodilatation, with a consequent rise in the pressure of the cerebrospinal fluid, so that the enlargement of the arteries is controlled and the headache abolished. The headache returns as the dilator effects of the second injection subside. It is, Pickering concludes, the action of histamine on the vessels which, by a mechanical disturbance, leads to headache; and the same explanation will probably account for the headache commonly found in maladies with high fever. It remains to be seen whether or not this is the explanation of other forms of headache.

THE PURPOSE OF DEEP PAIN

It has been seen that there is a close relation between skin pain and injury; in the survival of the species it has served a useful purpose in preparing the response to injury. On the other hand, if pain has any function in disease it is hidden from us. We cannot see that a man passing a minute calculus along the ureter is any the better for doing it in torment; nor is it revealed to us how the victim of cancer or a cerebral tumour benefits from his pain. Trotter concludes that so far as the interior of the body and disease are concerned, the mechanism of pain appears to be crude, ill-adapted and relatively functionless. Is this the final word on deep pain?

Hilton, in 1863, gave as the purpose of pain the need for resting the injured part, and a partial explanation of deep pain has been sought in the manner in which it discourages the use of the painful tissues. The pain in ischæmia, as in angina pectoris or intermittent claudication, appears to serve this purpose, but when the sensory nerves are cut in a patient with angina so that his exercise is no longer controlled by the appearance of pain, he does not seem to suffer from his new licence. We cannot explain the purpose of deep pain. We do not even understand why gross insults can be offered to viscera, such as clamping the stomach (so long as we do not pull on the mesentery), or pinching or pricking the heart without exciting pain. Gordon Holmes argues that it is not surprising that most of the viscera are insensitive to stimuli, cutting and burning, which excite pain in somatic structures as they are normally not exposed to such traumas, so that it is not to be expected that they would be endowed with a nervous apparatus to respond to them.

THE APPRAISAL OF PAIN

All successful physicians are good psychologists. Let the tyro in out-patients who rushes to the radiologist for help, watch the experienced physician at work as the long procession of dyspeptics without physical signs passes. How patiently he tests the credulity of a witness, with what care he analyses the evidence. Is this pain in the pit of the stomach pain at all, or only discomfort? Does it wake him at night? Can he feel the pain passing through to his back? With such questions the physician tries to sift those who have

PRESENT-DAY SURGICAL PRACTICE IN THE UNITED STATES

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WITHIN the past decade in the United States a great deal of attention has been directed toward the consideration of factors which influence wound healing.

WOUND HEALING

Because *vitamin C* is essential for the deposition of collagen, a deficiency of this vitamin greatly retards wound healing (Holman, 1940). Vitamin C deficiency is so common in prospective surgical patients that ascorbic acid is administered routinely pre- and post-operatively to persons requiring surgical procedures. The dosage administered is relatively large, ranging from 100 to 500 mgm. three times daily, depending upon the severity of an existing infection.

Also of great importance in wound healing is the maintenance of *normal serum protein balance*. It has been shown by Ravdin (1940) and others that a plasma protein deficiency interferes with wound healing because of excessive œdema at the wound site and increased incidence of infection. Lyons (1947) has shown, however, that even though by ordinary blood determinations the erythrocyte and leucocyte counts, the hæmoglobin and plasma protein values are within normal limits, actually there may exist a severe deficiency which will not be evident unless the blood volume is determined. In the chronically ill patient, particularly one who has lost weight, suffering either from infection or malignancy, the blood volume is likely to be contracted and, although the hæmoglobin and plasma protein values and the red cell count per cubic millimetre are within normal limits, the actual total amounts of circulating hæmoglobin, plasma protein, and red cell mass are deficient. A satisfactory method of determining blood volume is the Gregerson Evans blue technique, which is accurate enough for clinical use. George Whipple has shown that in hæmoglobin deficiency there is a preferential demand upon body proteins for the synthesis of hæmoglobin. It is therefore obvious that in a surgical patient whose total circulating hæmoglobin is less than normal, retardation in wound healing is likely because the proteins, which otherwise might be available for tissue repair, are utilized for the synthesis of hæmoglobin. It is important in all chronically ill patients, with either infection or malignancy, before undertaking any operative procedure to determine the blood volume, because only in this way can it be ascertained whether or not there is a deficiency in the total circulating hæmoglobin, red cell mass, and plasma protein. If a deficiency, particularly of hæmoglobin, exists, it should be corrected.

organic lesions in the belly from those who have only functional disturbances in their heads. Lewis, to be sure, was sceptical about the physician's capacity to measure pain, but he had not learnt in the hard school of private practice to cultivate insight into a patient's character. He was more versed in the science of medicine than in the art; the appraisal of personality fell outside his beat. But why quarrel with the search for an objective measurement of pain? Wayne, in testing therapeutic remedies, found that a certain patient could go up a number of stairs forty times before provoking cardiac pain, whereas after taking nitroglycerin he climbed the same stairs ninety times before he felt pain. The precision which we seek still seems a long way off; wrestling with symptoms, the physician gets little help from physical signs; the pulse may rise in severe abdominal pain; muscular rigidity may cast suspicion on an abdominal viscus; there may be signs of inflammation. But I speak against the rule.

Leaving the general physician among his dyspeptics, let me take you to the neurological department, where Dr. Gordon Holmes is shaping his examination so that he may be able to distinguish between organic pain and pain associated with hysteria or with malingering. Holmes demonstrates that the distribution and description of the pain are unlike those found in organic diseases. For example, a patient who complains of a tight band round his head has gone out of his way to make the task easy; no organic label fits. Holmes finds exaggerated tenderness in the painful area; he distracts the patient's attention and the tenderness disappears. Or the tender spot is carefully marked on the skin when, on approaching it from another direction, the position of the spot is found to vary. Or the patient's complaints are at variance with what he can do with a leg or arm if his attention is caught and diverted. The patient's inconsistency has betrayed him.

When we have failed to demonstrate organic disease, are we so certain that no structural abnormalities exist? The wise physician is conscious of his own frailty. The sane psychologist has a case when he pleads for a positive diagnosis which does not rest entirely upon the exclusion of organic disease. Such a diagnosis, H. L. Wilson argues, has the backing of symptoms, each in itself of no great moment, but together constituting a formidable body of circumstantial evidence. The patient's symptoms prevent him from doing something at work or play; the pain is preceded and not followed by emotional disorders or inexplicable exhaustion. He is prone to complain of his treatment in the past; he refuses to accept reassurance. The experienced physician, while he hunts for evidence of organic disease, is sensitive to the speech of a patient with a hurt mind; if he does not think in the patient's language as the psychiatrist does or should, he can freely translate it—and he does so every day of his life.

The references to Professor E. D. Adrian, Dr. Gordon Holmes and Dr. R. L. Wilson refer to the contributions by these authors in the series of articles on "Pain and its Problems", published in *The Practitioner* during 1947, of which the present article constitutes a summing-up.

is divided into two phases. Although the sulphonamides are more effectual in controlling the Wolff-Israel type of actinomycosis, their use in the acute phase of the infection is contraindicated because of their depressant effect upon the hæmopoietic system and the danger of aggravating the already existing anæmia. Penicillin, although not as efficacious in the treatment of actinomycosis, is used in the acute phase. Relatively large doses of 50,000 to 100,000 units every three hours are employed for ten days to two weeks until the acute infection is controlled. Following this, sulphonamides, particularly sulphadiazine, 4 gm. daily, are administered for many months, usually three to four months after all the sinuses have healed.

By this threefold attack it is possible to control practically all cases of actinomycosis.

ANTIBIOTICS IN PERITONITIS

Before the war the local implantation of sulphonamides into wounds was quite popular. Investigations conducted under the auspices of the National Research Council (Meleny, 1945) during the war demonstrated that sulphonamides were of doubtful value in the prevention of wound infection and that they were harmful when used locally. Because of this, the local implantation of sulphonamides has been abandoned. When sulphonamides are used in established infections they are administered systemically and not implanted locally, i.e. sulphonamides are no longer employed locally in peritonitis, which is now treated primarily with large doses of penicillin. Whereas theoretically penicillin should be of little value in the treatment of peritonitis, because it is relatively ineffectual against gram-negative organisms, it is believed that by controlling the growth of streptococci with adequate doses of penicillin the coliform organisms can be controlled by the natural body resistance. The doses of penicillin are large, from 500,000 to 1,000,000 units initially, with similar doses continued hourly for six hours, following which 200,000 to 500,000 units are given every two to three hours. Practically, it is possible to control most cases of peritonitis in this way. As a matter of fact, unless the contamination has been excessive, much smaller doses are required. Streptomycin also has been used in the treatment of peritonitis, and although its use is probably desirable in an extremely sick individual who is not doing well under penicillin therapy, it is not justified in the treatment of most cases of peritonitis because of its relative danger.

The preoperative administration of the sulphonamides in the preparation of patients with intestinal tract lesions is desirable. At present in the United States sulphathaladine is most frequently used and has the advantage over sulphasuxidine in that it does not produce irritation of the bowel and cause diarrhœa. It can be administered over relatively long periods of time, is poorly absorbed from the gastro-intestinal tract, and therefore is not likely to produce systemic damage. Recently Ravdin (1947) has administered streptomycin by mouth to patients who require surgical procedures on their intestinal tract and has been able to control the bacterial flora completely. Patients being prepared for intestinal surgery by the administration of the oral sulphonamides or streptomycin, should receive vitamin K, because the antibiotics are so effective in controlling the growth of intestinal flora that

This is best accomplished by the administration of whole blood. The amount of blood required to correct the deficiency in the chronically ill patient is much greater than ordinarily used and frequently is as much as two to four litres. With the introduction of this method of preoperative management it is now possible to prepare almost any patient, regardless of how ill he may be, within a short period of time for an operation of any magnitude. If during the operation sufficient blood is given to compensate for the blood lost, the patient will tolerate the procedure without any difficulty and operative shock can be completely eliminated.

Although emphasis has been placed upon the correction of any hæmoglobin deficiency by transfusion of whole blood, it is also important that if the patient is able to eat he should be fed protein and carbohydrates, because with the establishment of a normal total circulating hæmoglobin value the protein ingested can be utilized for tissue repair.

Another contributing factor in wound healing is the type of *suture material* employed. At present in the United States non-absorbable sutures are being used to an increasing extent. Non-absorbable sutures produce less reaction and, probably because of this, fewer infections occur in wounds closed with them than when absorbable sutures are used. The non-absorbable sutures which are popular are fine stainless steel wire, cotton, and silk. Steel is an excellent suture in that it is well tolerated by tissues, but has the disadvantage that it is more difficult to use than cotton or silk, is more likely to cut through, and is radio-opaque. Cotton and silk, because they are pliable, are easier to use than steel.

As shown by Ochsner and Meade (1940) cotton is tolerated much better by the tissues, particularly in the presence of contamination, than is silk and for this reason is preferred to silk. Although wound contamination is considered a definite contraindication to the use of silk, it is in no way a contraindication to the use of cotton. Sinus formation in infected cotton-closed wounds is infrequent and much less than in silk-closed wounds, probably because in the latter granulation tissue grows in between the separated silk fibres, whereas in cotton-closed wounds the twisted suture becomes so firmly twisted when wet by tissue fluid that ingrowth of granulation tissue between the cotton fibres is not possible.

-ACTINOMYCOSIS

Lyons and his co-workers (1947) have shown that severe actinomycosis can be treated satisfactorily if a combination of several methods of therapy is employed, the use of any one of which alone is likely to result in failure. The threefold attack consists of adequate surgical drainage, the correction of hæmoglobin deficiency, and the use of antibiotics.

Adequate surgical drainage is necessary in all cases of actinomycosis for the evacuation of necrotic material and to prevent residual pocketing. Lyons has shown that those patients who are chronically ill with a severe infection have a markedly contracted blood volume and a severe deficiency of total circulating hæmoglobin which may not be determined by the ordinary blood count. Unless the hæmoglobin deficiency is corrected, repair of the destructive lesion is not possible because the available protein is utilized for synthesis of hæmoglobin. Because of the anæmia resulting from the disease, so constant in actinomycosis, sulphonamides should not be administered during the acute phase of the infection because they, too, interfere with hæmopoiesis. The anæmia is best corrected by the administration of whole blood. The amount of whole blood necessary to correct the hæmoglobin deficiency is ascertained by the determination of blood volume. The treatment with antibiotics

most frequently complicates septic infections following criminal abortion, does embolism occur, and this is due to liquefaction of the clot as the result of the suppurative process. The emboli are particularly dangerous because they are infected and produce septic infarcts in the lung and sepsis. Although few persons with thrombophlebitis die, because the incidence of embolism is low, complications and sequelæ which follow true phlegmasia alba dolens are post-phlebitic œdema, post-phlebitic ulceration, and post-phlebitic streptococcal infection with elephantiasis.

The treatment of suppurative thrombophlebitis consists of ligation of the vein proximal to the site of involvement, and in the case of pelvic suppurative thrombophlebitis this consists of ligation of the vena cava above its bifurcation and ligation of the ovarian veins. The treatment of non-suppurative thrombophlebitis (typical phlegmasia alba dolens) is ultra-conservative. The symptoms in thrombophlebitis are the result of vasospasm and although the lesion is in the vein the clinical manifestations are caused by arteriolar contraction. The treatment therefore consists of overcoming the vasospasm, which can be accomplished satisfactorily by procaine anesthetization of the regional sympathetic ganglia. In the typical case of phlegmasia alba dolens the first, second, third, and fourth lumbar ganglia on the affected side are injected. Prompt relief of symptoms is obtained; there is complete disappearance of pain, rapid subsidence of fever, and diminution in the size of the extremity. By the prompt institution of conservative therapy subsequent sequelæ can be prevented.

Phlebothrombosis, which is unassociated with inflammation of the vein, is the result of two factors, increased coagulability of the blood, which is a predisposing factor, and circulatory stasis which is a precipitating one. The increased clotting tendency of the blood is the result of tissue damage. The cause of the tissue damage is immaterial. It may be accidental trauma, operative trauma, trauma during delivery, or destruction of tissue as a result of invasion by neoplastic disease or infection. Although the increased clotting tendency occurs in all parts of the vascular system, phlebothrombosis occurs almost without exception in the lower extremities. The localizing factor in the lower extremity is undoubtedly circulatory retardation.

The prophylactic treatment of phlebothrombosis therefore consists of minimizing the degree of tissue damage as much as possible and preventing circulatory stasis in those parts of the body in which stasis is likely to occur. Mobilization of the lower extremities by active muscular contraction, the use of compression bandages, deep breathing, in order to favour the return of the flow of blood to the heart by increasing the negative intrathoracic pressure, and early ambulation will minimize circulatory stasis. Although anticoagulants will prevent venous thrombosis they are probably too dangerous to be used routinely but should be employed prophylactically in patients who have clotting tendencies.

The diagnosis of phlebothrombosis is difficult because the patient has few or no symptoms. Unless patients confined to bed and who have had tissue injury are examined carefully for vein tenderness the first manifestation may be caused by pulmonary embolism. Tachycardia associated with tenderness of the calf or pain in the calf or popliteal space when the foot is forcibly dorsiflexed (Homans' sign) justifies a diagnosis of phlebothrombosis. The treatment of phlebothrombosis consists of ligation of the vein above the site of involvement or removal of the clot from the vein followed by ligation. The use of anticoagulants is increasing in the United

synthesis of vitamin K, which is the result of intestinal bacterial action, is obviated and prothrombin deficiency results.

HYPERTHYROIDISM

Thiouracil and propylthiouracil are of great value in the treatment of toxic thyroid disease. The latter has a distinct advantage over thiouracil in that it produces far fewer complications and can be used with relative safety over long periods of time. Although they have been used with inconstant results in the curative treatment of hyperthyroidism they are of great value in the preoperative preparation of these patients. Probably many cases of hyperthyroidism are better prepared with iodine, which has the distinct advantage over thiouracil in that the patient is prepared for the operation much more quickly, usually within ten days to three weeks instead of four to eight weeks required by thiouracil therapy. On the other hand, there are definite cases in which iodine therapy should not be used. The patient who has received iodine over long periods of time and who has become "iodine fast" will no longer respond to iodine and should be given thiouracil. Propylthiouracil is also indicated in patients in whom for some reason or other, such as pregnancy, an operation is temporarily contraindicated. Although a cure may not be obtained by the use of the drug, the toxic manifestations are controlled until thyroidectomy can be done because the drug produces at least a temporary chemical thyroidectomy. Propylthiouracil is also indicated in the treatment of thyrocardiac patients with toxic adenoma. The thyroid toxicity can be controlled readily by iodine administration but usually this therapy prepares the thyroid for operation long before the cardiac condition has improved sufficiently to withstand the operative procedure. In these cases it is better to use propylthiouracil, which requires a longer period of preparation and which permits the cardiac condition to improve sufficiently for the operation to be performed safely.

VENOUS THROMBOSIS

A subject of considerable interest to clinicians in the United States is venous thrombosis. Ochsner and DeBakey (1945) have emphasized the necessity of differentiating between two types of venous thrombosis, thrombophlebitis and phlebothrombosis, which are different in every respect except that in both instances a clot is present in the vein. They believe that unless these two types are differentiated the treatment is likely to be unsuccessful. The two types differ etiologically, symptomatically, prognostically, and therapeutically.

Thrombophlebitis, in which the thrombus is the result of an inflammation of the vein wall, is accompanied by symptoms—fever, swelling, pain, and tenderness of the involved extremity. The clot in thrombophlebitis is a white thrombus, and because it results from changes in the endothelium it is firmly attached to the vein wall and will not become detached to form an embolus. Only in the rare form of suppurative thrombophlebitis, which

most frequently complicates septic infections following criminal abortion, does embolism occur, and this is due to liquefaction of the clot as the result of the suppurative process. The emboli are particularly dangerous because they are infected and produce septic infarcts in the lung and sepsis. Although few persons with thrombophlebitis die, because the incidence of embolism is low, complications and sequelæ which follow true phlegmasia alba dolens are post-phlebitic œdema, post-phlebitic ulceration, and post-phlebitic streptococcal infection with elephantiasis.

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States, and although anticoagulants prevent further propagation of an already formed thrombus in phlebothrombosis there is no evidence that they in any way affect the existing clot. Dicumarol is a splendid anticoagulant but should not be used unless an adequate laboratory is available in order to control the prothrombin time. If employed in this way there is relatively little danger from its use. Anticoagulant therapy is indicated in patients with pulmonary infarction because it will prevent progression of the thrombus within the lung.

THORACIC SURGERY

Within the past decade there has been considerable interest in thoracic surgery. The treatment of *bronchogenic carcinoma* has become so well standardized that the operation of pneumonectomy can be done with relatively little danger. The results from pneumonectomy have been quite satisfactory. Ochsner, DeBakey, and Dixon (1947) have recently reported a five-year survival rate of 23 per cent. following pneumonectomy. This is particularly significant because in many of the cases which these investigators operated upon only a palliative resection was done, a procedure which is considered as justified in bronchogenic carcinoma as in carcinoma of the stomach or colon. The results at the present time following pneumonectomy for bronchogenic carcinoma are much better than those following gastrectomy for gastric carcinoma. It is significant that although in the United States as a whole, of the cases admitted to hospitals and in which a diagnosis of gastric cancer was made, only 5 per cent. are alive at the end of five years, in a group of cases of bronchogenic carcinoma similarly studied by Ochsner, DeBakey, and Dixon (1947) 8 per cent. are alive at the end of five years.

The treatment of *benign neoplasms and suppurative lesions* of the lung has also become standardized. In bronchiectasis and in lung abscess much has been accomplished by conservative resection of the lung. Whereas previously a lobectomy was frequently resorted to when only a portion of a lobe was involved, now segmental resection of the involved portion of the lobe is done. In this way it is possible to do more radical surgery by conserving those portions of the lung not involved.

BURNS

The treatment of burns has become standardized. Tannic acid, which was so popular before the war, has been shown to be detrimental not only because of the eschar produced which interferes with drainage in the presence of infection, but also because tannic acid absorbed from the wound surface causes severe liver damage. Tannic acid and other escharotic agents have been completely abandoned (McClure *et al.*, 1944). The care of the burned patient has been placed on a rational basis in that the burn is treated as a severe wound.

The local treatment consists of careful gentle cleansing of the burned area, using aseptic precautions, followed by the application of sterile dressings and compression bandages which produce partial immobilization. Unless otherwise indicated the

initial dressings are left undisturbed for two to three weeks. The systemic treatment of the burned patient consists of administration of large amounts of blood. Coller and his associates (1940) have shown that even though hæmoconcentration may exist, the administration of whole blood is necessary to prevent death in the severely burned individual. In order to prevent hypochloræmia, which is likely to result from excessive exudation, chlorides are administered by mouth but not intravenously. Connor and Harvey (1944) have shown that the eschar complicating third degree burns can be removed quickly by the application of pyruvic acid to the burned area. The necrotic tissue separates within two to three days leaving a clean granulating surface that can be grafted early.

CONGENITAL HEART DISEASE

The safe surgical correction of congenital cardiac defects, particularly patent ductus arteriosus and the pulmonary stenosis in tetralogy of Fallot, is now possible. *Patent ductus arteriosus* should be corrected either by ligation or by division and suture, preferably the latter. Blalock (1946) suggested circumventing the stenotic area in the pulmonary stenosis of *tetralogy of Fallot* by anastomosing the end of the subclavian artery to the side of the pulmonary artery. This procedure, although it does not cure the patient in that subclavian pulmonary shunt is not normal, can be performed safely, greatly improves the patients and prolongs their lives by relieving their anoxia. *Coarctation of the aorta* is best treated by excision of the stenotic segment and anastomosis of the two ends of the aorta. In cases in which excision and anastomosis are not possible, a shunt around the stenotic area by anastomosing the left subclavian artery to the aorta distal to the stenosis gives some relief, but does not effect a cure.

THE ŒSOPHAGUS

Surgery of the upper gastro-intestinal tract has made great strides.

Adams and Phemister (1938), Sweet (1945), Garlock (1944), and Ochsner and DeBaKey (1941) have shown that extirpation of extensive portions of the œsophagus is possible with the re-establishment of the continuity of the upper digestive tract by mobilizing the stomach into the chest and anastomosing it to the œsophagus high in the thorax. In this way, highly located lesions, even those behind the arch of the aorta and above, can be removed with transthoracic re-establishment of the continuity of the digestive tube. Benign strictures resulting from cicatricial narrowing of the œsophagus following chemical cauterization are also satisfactorily corrected by this procedure. Recently Phemister (1947) has suggested that severe œsophageal varices associated with portal hypertension complicated by repeated exsanguinating hæmorrhages can be corrected by resection of the distal œsophagus and proximal stomach, followed by œsophagogastrostomy in order to remove the dilated varicosities. Although this is an heroic procedure, it is justified in the patient who does not respond to conservative therapy such as injection of the œsophageal varices with sclerosing agents, which has been popularized by Moersch (1941). Moersch (1947) has recently suggested that the injection treatment is particularly indicated in those cases in which the varicosities are limited to the œsophagus but should not be used in cases in which the varicosities extend to the stomach. In this latter instance probably some other procedure is necessary, such as a shunt between the portal and caval systems, either as an anastomosis between the portal vein and the inferior vena cava or as an anastomosis between the splenic and renal veins, as suggested by Whipple (1945) and Blakemore and Lord (1945). The results from the portal caval shunt leave much to be desired.

PEPTIC ULCER

There has been a great deal of enthusiasm concerning the use of *vagotomy* in the treatment of duodenal ulcer, but at the present time the enthusiasm is somewhat waning because of many bad results which have followed this procedure. Dragstedt (1945) remains an ardent advocate of the procedure and believes that it is the one treatment for duodenal ulcer. Other investigators who have had considerable experience with the procedure are becoming less enthusiastic than they were previously. Moore (1947), Grimson (1946-47), and Walters (1947), although still using vagotomy in the treatment of duodenal ulcer, are much more conservative in their indications. The fear has been expressed by many that, although the results are dramatic immediately following resection of the vagi, one cannot predict what is going to happen to these patients after considerable time has elapsed, and there is fear that the disturbed gastro-intestinal physiology resulting from wide resection of the vagi may cause troublesome sequelæ. Generally, in the United States, the chronic duodenal ulcer which does not respond to conservative therapy is treated by subtotal gastric resection.

Although conservatism is indicated in the treatment of duodenal ulcer, it is the opinion of most gastric surgeons that *gastric ulcer* should be treated radically because of the impossibility of determining whether malignant change has already occurred, and also because of the chance that the lesion may become malignant later on. The gastric mucosa is so susceptible to malignant change that to permit a gastric lesion to exist for a long period of time is dangerous because of the chance of malignant transformation. Until apparently non-malignant gastric lesions are treated radically the salvage rate in gastric carcinoma will continue to be low and can be increased only by treating gastric lesions when a diagnosis of gastric carcinoma cannot be made.

ACUTE CHOLECYSTITIS

Whereas there has been considerable controversy in the past concerning the advisability of early or late operation in acute cholecystitis, more surgeons are beginning to believe that because acute cholecystitis begins first as a mechanical obstruction and infection is relatively late, the gall-bladder should be removed soon after the onset of symptoms, before bacterial invasion of the gall-bladder has occurred.

Ochsner, Johnston, and Brunazzi (1948) have shown in a series of cases observed at the Charity Hospital in New Orleans that the mortality rate was low when patients were operated upon within seventy-two hours of the onset of the disease. If operation was done between the third and seventh days the mortality rate was high, but the mortality rate was also low when operation was performed after the seventh day of onset.

It is thus evident that the results from the surgical treatment of acute cholecystitis more or less parallel the results in acute appendicitis. Ideally, the gall-bladder should be removed within the first three days of the onset of symptoms, because during this phase the inflammatory process is the

result of mechanical obstruction and chemical irritation. Only later, bacteria invade the wall of the gall-bladder, and when this occurs the risk is greatly increased.

HYPERTENSION

The surgical treatment of hypertension is popular at the present time in the United States. Although there is some controversy concerning the extent of the operation which should be done, the reported results consistently have not been ideal. The operation is worth while, however, in that it does ameliorate symptoms in practically all patients and produces a permanent falling of the blood pressure in from one-fourth to one-half of the cases. Unfortunately, slightly less than one-half of the patients operated upon are not benefited at all except that their symptoms are relieved. Since these patients, however, can be offered nothing else so far as therapy is concerned, these results, although not everything to be desired, are acceptable.

HÆMOSTATIC AGENTS

There are available at the present time hæmostatic agents which are of great value, particularly in controlling hæmorrhage from parenchymal surfaces. The three substances which are used are fibrin foam, gelatin foam, and oxidized cellulose. Gelatin foam has the advantage over fibrin foam in that it has somewhat more body than fibrin foam and is therefore easier to use. It produces about the same amount of reaction as does fibrin foam, and because it is much more readily produced it is much cheaper and is preferred. Oxidized cellulose is also an effective hæmostatic agent. Not only does it serve as a tampon, but it also exerts a hæmostatic effect. Large oozing surfaces can be readily controlled by the application of one of these substances. Bleeding associated with injuries to solid viscera, such as the liver, can be readily controlled by their use.

RECTAL SURGERY

At the present time there has been some revival of attempts to conserve the sphincter in low-lying lesions of the rectum and recto-sigmoid. Although twenty-five years ago there was a good deal of controversy, particularly in Europe, concerning the advisability of preserving the anal sphincter in low-lying colonic lesions, experience has shown that attempts to preserve the sphincter caused a high incidence of local recurrence.

Following the investigations of Gilchrist and David (1938) and Coller, Kay and McIntyre (1940), in which it was shown that the principal spread in malignancy of the colon was upward, there was a revival in these cases of the conservative operation with re-establishment of continuity of the bowel and the abandonment of the abdomino-perineal resection. Although the conservative procedure has some advocates in the United States, most surgeons believe that abdomino-perineal resection, the classical Miles procedure, is preferable in these low-lying lesions and that to compromise with malignancy will mean a higher incidence of recurrence and a higher fatality rate. Lahey (1948), and Ochsner (1946), amongst others, are definitely opposed to the conservative operation in low-lying lesions because an

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CURRENT THERAPEUTICS

II.—CURARE AND CURARE-LIKE DRUGS

By ARCHIBALD D. MARSTON, M.R.C.S., D.A.

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THE securing of adequate muscular relaxation, which has always presented a difficult problem, has been produced by (1) deep inhalation anaesthesia; (2) transient suboxygenation, as effected by McKesson's technique of secondary saturation; (3) various forms of analgesia, of which local infiltration, and regional, subarachnoid and epidural blocks are the most widely practised. But all these methods have had certain disadvantages as regards the patient's well-being. Thus when Griffith and Johnson (1943) achieved relaxation by curarization of muscle, this method was hailed with enthusiasm by many, and certainly secured the interest of all anaesthetists.

Some little time has elapsed since the introduction of this epoch-making innovation, and views as to its value vary. Gray and Halton (1946), who have employed curarization in over 2000 cases in Liverpool, have formed a high opinion of its value and favour its routine use. On the other hand, many anaesthetists have expressed less favourable opinions. Experience has shown that curare is only safe in the hands of the anaesthetic specialist and should on no account be used by those not fully conversant with its action.

According to Dewing (1947), curare has also been described as woorari and woorali by various explorers in their attempt to express phonetically the native name of this drug, which was first reported by Sir Walter Raleigh in his voyage of discovery to Guiana in 1595, and was mentioned by Hakluyt in his interesting book a few years later. Curare was used by the natives inhabiting the wild country between the Amazon and Orinoco rivers for the poisoning of the tips of arrows fired from blow-guns used in hunting animals. Crude curare is an extract of several species of tropical liane and is a brown syrup-like substance with a bitter taste and an odour resembling that of liquorice. It contains a variety of alkaloids and is unsuitable for clinical use in its crude state. The natives pack the crude curare in small clay vessels (pot curare), in calabashes (gourd curare), and in bamboo tubes (tube curare). Much investigation has been carried out in an endeavour to discover the precise botanical origin of the three varieties, and also to identify the alkaloid responsible for curarization of muscles.

d-TUBOCURARINE CHLORIDE

Following the work of King in 1935 helped largely to elucidate these problems, and the colon was generally accepted that *d*-tubocurarine chloride is the alkaloid with re-establishing abdominal-perineal advocates in the resection, the clean product which is probably prepared from the plant species *Menis-* that to compromise and a higher fatal definitely opposed.

insufficient amount of bowel is likely to be removed and the incidence of local recurrence will be high.

Undoubtedly one of the reasons why there has been a revival of this once discarded procedure is because with the use of antibiotics the bowel can be prepared satisfactorily so that it can be operated upon safely with relatively little danger of contamination. The incidence of complications, however, in addition to the incidence of recurrence is much higher than in those cases in which the abdomino-perineal resection is done.

The sooner physicians and patients realize that a colostomy is no bugbear, the sooner the Miles procedure will be accepted. Unfortunately, too few people pay attention to the care of the colostomy and this has given the abdominal colostomy a bad name. It is far better not to use colostomy bags but to teach the patient how to care for his colostomy and, in this way, teach him how to obtain an evacuation of his bowel every forty-eight to seventy-two hours. At other times he can be perfectly free from symptoms and will have no difficulty with his colostomy.

affected for two hours or more. If the dose of tubarine is sufficiently strong to paralyse the diaphragm this effect takes place within ten minutes of intravenous injection and may be treated by artificial ventilation of the lungs.

The action of tubarine varies in different individuals. If its effects are too great, then prostigmin may be used as an antidote. The usual dose of prostigmin is from 1-2 mgm., but Prescott (1947) recommends higher doses and also the addition of atropine to counteract undue stimulation of the parasympathetic nervous system.

Effects on respiration.—Gray (1947) draws attention to the fact that whenever complete relaxation of the abdomen is secured by curarization the intercostal and diaphragm muscles are also affected to a varying degree. The patient continues to breathe regularly but not so efficiently, and clinical symptoms of imperfect ventilation of the lungs become apparent, such as a raised blood pressure and an increase of capillary hæmorrhage from cut surfaces. This state of affairs predisposes to pulmonary collapse and other untoward postoperative respiratory complications. This effect of tubarine and intocostin is perhaps the crux of much of the opposition by many anæsthetists towards any routine use of these drugs.

In skilled hands much of this respiratory depression may be countered by the use of smaller doses and also by the adequate administration of oxygen accompanied by ventilation of the lungs by positive pressure when required.

Organe (1947) gives details of a series of 86 abdominal operations in which no less than 39 of the patients developed postoperative chest complications, such as lobar collapse, broncho-pneumonia, subphrenic abscess with pleural effusion, pulmonary infarction, and febrile coughs with copious sputum. Massey Dawkins (1947) describes 50 gastrectomies relaxed with curare, of which 20 per cent. developed collapse of the base of the lung as confirmed by radiological examination.

Experiments in dogs by West (1935) and others have revealed the existence of *bronchospasm*, but in the case of West's researches a curare product other than intocostin or tubarine was used and this effect may thus have been due to another alkaloid. Prescott (1947) believes that bronchospasm may occur in a conscious or lightly anæsthetized patient if the dose of the curarizing drug is small.

John Gillies (1947) described the case of an infant aged eight weeks who died three-and-a-half hours after an operation during which 5 mgm. of *d*-tubocurarine chloride were used to secure total paralysis of muscles, including the diaphragm. Post-mortem examination revealed complete collapse of both lungs.

Organe (1947), in a group of 59 upper abdominal operations with curarization, records that 11 out of 15 intubated patients developed chest complications compared with 20 out of 44 not intubated, and suggests the possibility of a reflex bronchospasm. It is known that pentothal may cause spasm, and also that curare potentiates the action of this drug, whilst the additional stimulus of an endotracheal tube may well account for this untoward effect. Mountford (1947) has recorded a fatal bronchospasm following attempted

permacæ. According to Dutcher, *d*-tubocurarine has actually been extracted from the liane, *chondrodendron tomentosum*, but Dewing observes that this work at present lacks confirmation. Tube curare contains the quaternary ammonium salt, *d*-tubocurarine chloride, and also a toxic tertiary base known as curine.

Tubarine and intocostin.—King (1935) elaborated a technique for the successful extraction of *d*-tubocurarine chloride as a crystalline alkaloid, and it is now available for clinical use in a stable solution known as tubarine, containing 10 mgm. per c.cm., and prepared by Burroughs Wellcome & Co.

Intocostin (Squibb) is the proprietary name of an extract of crude curare which is much used in North America and has a different dosage from tubarine. It is prepared from the *chondrodendron tomentosum* and contains a high percentage of *d*-tubocurarine. Prescott (1947) has stated that intocostin owes its curariform action almost entirely to this fact.

The relative potency of the two drugs as regards curarization of muscle has been carefully estimated by contemporary pharmacologists by experiments on small animals, 6.67 units of intocostin being equal in action to 1 mgm. of pure *d*-tubocurarine chloride (Prescott, 1947). But in clinical use the dose is probably more in the region of 3.0 to 3.3 units of intocostin to 1 mgm. of the pure alkaloid (Prescott, 1947), and according to Gray (1947) 1 mgm. of intocostin has the effect of 0.2 mgm. of tubarine. In this country tubarine is the preparation most often used, and is considered by many anaesthetists to be more reliable. Barnett Mallinson (1947), however, fails to observe any different effects of the two preparations.

Pharmacology.—Nearly one hundred years have passed since Claude Bernard, in 1857, carried out experiments on frogs and formed the opinion that the production of transient paralysis of muscle by a solution of crude curare was due to a blocking of nerve impulses at the myoneural junction. Much research has confirmed this opinion, and it is generally accepted that this failure in conductivity of nerve impulses is due to an interference with the normal action of acetylcholine. As is well known, acetylcholine is liberated at the myoneural junction during normal nervous impulse to muscle, but the presence of curare inhibits this effect. Once the effect of *d*-tubocurarine has passed off, both muscle and nerve resume their normal function and the myoneural junction is not damaged in any way.

Unless massive doses are given, the drug when administered by mouth produces little or no effect in man, since it is excreted rapidly. The usual practice is to inject tubarine intravenously. Its effect is observed to begin within a minute and to attain a maximum within five minutes. The muscles around the eyes and in the face and neck are first affected and then the muscles of the limbs, back and abdomen, and finally the intercostals and diaphragm (Prescott, 1947). The length of action depends upon whether the tubarine has been supplemented by inhalation anaesthesia, in which case the effect is potentiated. If given therapeutically, the limbs usually recover in thirty to forty minutes, whereas the muscles of the eye may be

should not be used in the presence of ether, as it increases the risk of pulmonary complications.

(3) Liver and kidneys: The drug is speedily metabolized and there is no evidence of any harmful effect on these organs.

Contraindications.—These are few, and in the opinion of most observers may be limited to myasthenia gravis, chronic respiratory obstruction, and myocardial degeneration with signs of definite cardiac embarrassment.

Dosage and administration.—In my opinion the best solution of *d*-tubocurarine chloride is tubarine (Burroughs Wellcome & Co.) which is stable to heat and is supplied in ampoules containing 15 mgm. in a strength of 10 mgm./c.cm.

Like most other drugs, tubarine has more effect on some individuals than others, and it is recognized that the aged, the feeble and the young usually require a smaller dosage. In the case of children, Gray (1947) advises for induction a dose of 2 mgm. per stone of body weight, whilst in the case of adults he recommends a divided dose, giving 5 mgm. intravenously in the conscious state, noting the reaction over a period of three minutes, and then giving a further 10 mgm. immediately before inducing anaesthesia with an intravenous barbiturate. An endotracheal tube or airway is then passed and the patient is put into a closed-circuit apparatus so that oxygen may be supplied and respiration assisted by rhythmic compression of the gas-bag, if required. As tubarine has a cumulative effect, smaller doses of tubarine are given as indicated during the course of the operation. Halton and Gray have devised an apparatus for continuous intravenous injection of tubarine and pentothal which enables the two drugs to be given without mixing, thus avoiding a precipitation in the pentothal.

In using this technique the intravenous injection is supplemented by cyclopropane and oxygen in the closed circuit. Towards the end of the operation this is increased, so that the patient is returned to bed largely free from any curarization effects. In my opinion the good results which have attended the large series of Gray and Halton are mainly due to this last precaution, to their meticulous care in avoiding overdosage and anoxia, and to the employment of assisted respiration without delay whenever required.

An alternative method is to induce with pentothal, secure an adequate airway, give an inhalation anaesthetic supplemented by pentothal as desired, and administer 7 to 10 mgm. of tubarine two minutes before the peritoneum is opened, observing the effect and adding small doses of tubarine as required.

MYANESIN

Thirty-seven years have passed since Gilbert and Descomps in 1910 described experiments on guinea-pigs in which, after injection with α -phenyl ether of glycerol, transient muscular paralysis was observed. This effect was confirmed by Lannoy.

Myanesin has been produced after a systematic investigation of the

intubation under pentothal alone, and suggests cocainizing the larynx and trachea before intubation when pentothal or tubarine is to be used.

Effects on heart and blood pressure.—According to Gray (1947), experiments on animals revealed little or no change in cardiac efficiency or venous pressure, an opinion which has clinical confirmation in records of over 2000 cases at Liverpool (Gray and Halton, 1946).

In the opinion of most clinical observers, curarization does not have any harmful effect on the cardiovascular system when used in correct dosage; but in the presence of anoxia and degeneration of the myocardium, fall of blood pressure and collapse have been recorded. Excessive bleeding from wound surfaces has been noted by many observers, including Dawkins (1947).

Effects on the gastro-intestinal tract.—Relaxation of the musculature of the small intestines has been demonstrated by Gross and Cullen (1945) in experiments on dogs. I have asked the opinion of many surgeons on this important clinical point, and there seems to be no unanimity. A small minority report constant inconvenience from dilatation, whereas the majority find no cause for complaint but often remark that relaxation has been observed in isolated instances. According to Griffith (1944), contraction was usually observed when cyclopropane or nitrous oxide gas was used with *d*-tubocurarine chloride. Obviously premedication and general anaesthesia often predispose to dilatation, and the potentiating effect of the curarizing agent may increase this tendency.

Cases of sudden precipitate vomiting have been reported in which inhalation has followed with a fatal result. Gray (1947) states that this is due to abnormal relaxation of the oesophageal muscle and sphincters and considers it to be one of the main dangers in the use of *d*-tubocurarine chloride.

Effects on the central nervous system.—Much research on small animals has revealed no definite opinion on this matter, but experiments on male volunteers have enabled Prescott (1947) to declare concisely that "*d*-tubocurarine chloride has no significant central stimulant, depressant or analgesic action in man".

Effects on shock-like states.—Although no definite scientific evidence has been advanced to explain any shock-sparing effects of *d*-tubocurarine chloride, there are in the opinion of many observers clinical grounds for such a possibility. Forrester (1947) reports that after viewing the effects of *d*-tubocurarine on 500 cases in Glasgow, he was impressed by the improvement in the condition of shocked patients and emphasizes the necessity for adequate curarization in order to attain a maximum benefit.

Miscellaneous effects.—(1) Salivation: As the drug definitely increases salivation, an adequate dose of atropine sulphate 1/100 to 1/50 grain (0.65 to 0.97 mgm.), should always be given.

(2) Effects on other anaesthetic agents: One of the most valuable effects is a potentiation, which is especially marked in the case of pentothal, ether and cyclopropane. In the opinion of several authorities full doses of curare

during the progress of the operation. The second and more common practice is to secure induction by intravenous pentothal or inhalation anæsthesia, the myanesin being given one to two minutes before relaxation is required and being repeated when necessary.

Using the second method, I have been impressed by the small amounts of myanesin required to secure relaxation in many abdominal operations. Quite often all that is required has been secured by giving 5 c.cm. just before the peritoneum is opened, and another 5 c.cm. just before it is closed. Perhaps the use of small doses has explained the freedom from untoward effects which has been experienced in an extensive series of cases.

Clinical aspects.—Many anæsthetists will agree with Barnett Mallinson (1947) in his conclusion that "curarization has come to stay, and I think myanesin will supersede curare for this purpose because of its far greater margin of safety and its simple organic synthesis". But, on the other hand, two effects of myanesin, which have been reported by many observers, must be mentioned; these are the possibility of venous thrombosis and the occasional occurrence of hæmoglobinuria.

Enderby and Pugh (1947) have reported three cases of hæmoglobinuria, and Stephen and Chandy (1947) the occurrence of 10 similar cases in a series of 50 administrations. In all cases the symptoms developed within a few hours and were not repeated in subsequent investigation.

Opinion varies as to the cause and frequency of venous thrombosis. Barnett Mallinson (1947) reports complete freedom from this complication and draws attention to the possibility of pentothal being the cause, whilst Stephen and Chandy (1947) record 7 cases of localized thrombophlebitis in a series of 50 administrations, and mention that all the patients recovered within forty-eight hours.

CONCLUSIONS

It is evident from this account of the use of curare and curare-like drugs that no complete evaluation of their benefits can yet be made; but few will deny the fact that they are a most valuable addition to the anæsthetist's armamentarium.

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pharmacological properties of α -substituted ethers of glycerol by the research department of The British Drug Houses Ltd. No less than 143 compounds were examined and most of them produced transient relaxation and paralysis of skeletal muscles in small animals. Myanesin was finally chosen as the compound which was potent and had a large margin of safety between paralysing and lethal doses (Berger and Bradley, 1946).

Chemical and physical properties.—Myanesin has the formula α : β -dihydroxy- γ -(2-methyl-phenoxy)-propane and is a pure crystalline synthetic substance. It is a colourless, odourless solid, and solutions of the drug are stable, can be sterilized by heating, and mix freely with sodium chloride, glucose, and derivatives of barbituric acid and thiobarbituric acid. This last property is especially valuable as it enables the drug to be used with an intravenous saline or glucose drip. It can also be mixed freely with pentothal in order to secure a speedy induction of anaesthesia with a degree of muscular relaxation which facilitates intubation.

Pharmacological effects.—The researches of Berger and Bradley (1946) show that the drug is comparable to tubarine in the speed of its metabolism.

Effects on the central nervous system.—Myanesin produces its muscular relaxation by diminution of the reflex excitability of the spinal cord. Relaxation of the abdominal musculature is attained by moderate doses and is not accompanied by marked depression of the tidal air. In fact, myanesin does not cause respiratory arrest even in completely paralysing doses.

Effects on blood pressure.—In experiments on rabbits and cats (Berger and Bradley, 1946) moderate doses had no effect on blood pressure, but massive doses caused a fall which returned to normal after a few minutes.

Toxic effects.—In order to investigate chronic toxicity, Berger and Bradley (1946) fed growing rats for over two months with a diet containing 2 per cent. of myanesin. Post-mortem examination revealed calculi in the bladders of 30 per cent. The kidneys, liver, spleen, lungs, heart and suprarenal glands did not reveal any naked-eye or microscopical abnormality.

Other effects.—Myanesin does not stimulate salivation or produce bronchial spasm, nor is its action cumulative as regards muscular relaxation. This drug potentiates the action of pentothal sodium and other derivatives of barbituric acid. According to Barnett Mallinson (1947), no obvious effect is usually observed on the tone of the musculature of the gastro-intestinal tract; but he mentions one case in which muscular tone was diminished. I have seen several similar cases, but in the opinion of most observers this is a rare occurrence.

Administration and dosage.—Myanesin is supplied in ampoules of 10 c.cm. containing 1 gm. of the drug. An intravenous dose of 5 to 10 c.cm. takes about one minute to develop muscular relaxation, which will continue for twenty to thirty minutes. Two methods of induction are commonly practised:—

In the first method, myanesin, 5 to 10 c.cm., is combined with enough pentothal sodium to secure anaesthesia, further 5 to 10 c.cm. doses being added as required

skin. If the colostomy does not act normally by the fourth postoperative day, a mild aperient, such as senna or cascara, is given. Strong aperients should be avoided as they cause distressing diarrhœa.

The dietary regime.—During the immediate postoperative period small quantities of fluid are given by mouth; if required this is supplemented by intravenous infusion. The diet is increased gradually when intestinal peristalsis returns and the colostomy begins to act. Food substances which produce a large amount of gas or irritate the bowel and cause diarrhœa must be eliminated, for the object is to promote easy action of the colostomy and avoid colostomy distress. The three main meals of the day can be chosen from the following menus, although under present austerity conditions the colostomy patient must not expect to be exempt from the restrictions applicable to the rest of the population.

Breakfast.—Juices: orange, grapefruit, tomato.

Fish: steamed.

Eggs: boiled, poached, shirred, buttered.

Omelette—plain, au confiture.

Bacon.

Rolls, toast, rusk.

Strained honey.

Coffee, fresh milk, tea.

Luncheon.—Fish: poached, boiled.

Eggs: shirred. Omelette.

Chicken; lamb; tenderloin steak; lamb kidney; sweetbread

Potatoes: boiled, mashed, baked.

Shredded lettuce.

Custard pudding. Ice cream. Jelly.

Rolls, toast.

Coffee.

Dinner.—Tomato juice.

Smoked salmon.

Fish: boiled, broiled.

Lamb; chicken; turkey; game.

Liver.

Potatoes: boiled, mashed, baked.

Shredded lettuce.

Biscuit glacé. Ice cream. Custard pudding.

Coffee.

The patient learns which articles of diet to avoid and he can experiment with various types of food. As progress is made other foods can be added to the diet, including more vegetables and fruit. He will soon learn to regulate his dietary requirements according to the above schedule and it is necessary to explain this subject to him.

MANAGEMENT BY THE PATIENT

Care of the colostomy.—The skin of the anterior abdominal wall around the colostomy is protected by a thin layer of zinc cream or vaseline. The bowel is protected from friction by placing over it a layer of gauze lightly impregnated with vaseline. The patient should pass the index finger, covered with a finger stall and lubricated, into each limb of the colostomy once a week.

Colostomy belt.—There are a number of satisfactory belts available. The belt is made of fabric, with an inner protective lining for that portion which covers the colostomy; it should have a fulcrum band with an anterior broad piece which affords excellent support to the anterior abdominal wall. A shallow celluloid plate can be incorporated which will fit over the colostomy and give added strength; alternatively, an oval piece of cardboard moulded to lie over the colostomy is quite satisfactory. A rubber cup should never be worn over a colostomy on account of the suction action which it produces. During the night the colostomy is covered by a layer of vaselined gauze and cotton-wool which is held in position by a bandage, or a light belt can be worn.

REVISION CORNER

THE MANAGEMENT OF A COLOSTOMY

THE institution of a fistula whereby the excretions of the body, whether faecal or urinary, can escape freely on the surface, is an event of considerable importance in the life of a patient, and the advice that it is necessary may cause considerable apprehension. This will be allayed, however, if the situation is presented to the patient in a way which is calculated to allay his fears, and a more enlightened view will be taken concerning the presence of a colostomy. In the management of a colostomy the surgeon and the patient play important parts and full cooperation must be established.

MANAGEMENT BY THE SURGEON

Some general observations.—A colostomy may be temporary, for example, when diversion of the faecal stream is required proximal to a partial colectomy with anastomosis or a vesico-colic fistula. A permanent colostomy is established in cases of inoperable carcinoma of the rectum, or when an abdomino-perineal excision of the rectum is performed. The permanent colostomy is the subject matter here.

The question is often asked "when should a permanent colostomy be established in the presence of an inoperable carcinoma of the rectum?" We can turn for the answer to Miles, whose words were backed by his great experience: "From what I have seen of these cases I am convinced that, as soon as carcinoma of the rectum is found to be inoperable, every day lost before resorting to colostomy is a day to the bad". A study of the pathological factors involved in this disease leads to the conclusion that this is right, for thereby the patient is absolved from the risk of certain supervening complications of an inflammatory or obstructing nature.

It must be realized that the operation carries a mortality risk, as these patients are in a poor general condition. Therefore careful preoperative preparation is essential, with the correction of nutritional defects, including secondary anaemia, protein deficiency and dehydration. The bowel is cleansed with a simple enema on alternate days until the day preceding the operation, and a course of sulfasuxidine is given, 3 gm. orally every four hours for four days.

The surgeon must explain to the patient exactly what the institution of a colostomy entails, and reassurance is given regarding its effects on his usual way of living and work. It is a help if examples of people with colostomies are given, for this will engender confidence. The patient is assured that he will be taught the details of colostomy management after the operation and be fitted with a good belt.

In performing the operation it is necessary to remember certain technical points so that troublesome postoperative complications are avoided.

I always use a left oblique muscle-splitting incision as this is directly over the pelvic colon, which can be delivered into the wound with ease, and prolapse of the small intestine appears to be less common through this incision. It is advisable to excise an ellipse of skin to prevent the development of subsequent stenosis. The peritoneal space in the outer side of the pelvic colon is closed with sutures to prevent a loop of small intestine prolapsing in this position and becoming strangulated. Care must be taken that a good spur is formed and a glass rod $3\frac{1}{2}$ inches long and $\frac{3}{8}$ of an inch in diameter with smooth round ends is passed through the meso-colon in an avascular area, the ends being joined by a half-circle of rubber tubing. This is left in position for a period of two weeks and is replaced by a rubber tube for one week. The ends of this rubber tube are turned over and bound with thread to prevent the tube from slipping out.

Immediate opening of the colostomy is advocated using a cautery; longitudinal and transverse incisions are made in the bowel so that the aperture is adequate. The skin around the bowel is covered with gauze impregnated with vaseline, which also affords firm support. A piece of oiled silk is placed over the colostomy together with a covering dressing which is held in position by a bandage.

During the period of healing it is advisable to pass the index finger into each limb of the colostomy several times a week to prevent stenosis occurring at the level of the

is found in "shock", whether following trauma, or hæmorrhage, or some acute accident such as perforation of an abdominal viscus, and in the critical phases of acute infections such as pneumonia, typhoid fever, and typhus. The mechanism responsible varies in different illnesses, but failure of peripheral vascular tone and sometimes, as after hæmorrhage, a lowered blood volume are important. The blood pressure is an index of the severity of the illness and a valuable guide to prognosis, and usually indicates a fatal termination if it persists for long below 90 mm. Hg.

Chronic debilitating diseases, such as pulmonary tuberculosis and carcinomatosis, are often associated with low blood pressure. So, too, are other conditions in which loss of weight is prominent, such as starvation, anorexia nervosa, and chronic intestinal disease with fluid loss and defective food absorption, such as sprue, dysentery, and ulcerative colitis. In the early stages of these illnesses the blood pressure is usually between 110 and 100 mm. Hg, but it may fall further as the disease progresses and hence it will be a sign of some prognostic value. Similar blood pressures are found in schizophrenics. In anæmia the systolic pressure may be lowered but seldom falls below 100 mm. Hg, although diastolic pressures may be greatly reduced. In this group peripheral mechanisms are probably also at fault.

Endocrine deficiency, especially of the suprarenal cortex and the anterior pituitary, is often associated with a low blood pressure. In Addison's disease (suprarenal deficiency) low blood pressure may be the outstanding physical sign, and systolic levels of less than 100 mm. Hg can be found even in periods of relative remission, whilst in a crisis they will be lower and often an indication of circulatory failure. In Simmonds' disease (anterior pituitary deficiency) and in severe myxœdema the blood pressure is often lowered but less so than in Addison's disease. The changes are in part the result of diminished blood volume. Although low blood pressure may be characteristic of these diseases it should not by itself be regarded as diagnostic in the absence of other supporting signs.

Heart disease is not often a cause of low blood pressure and even in severe failure normal levels are likely to be maintained, since until the terminal stages any fall in the cardiac output is compensated by the peripheral mechanism. A low blood pressure is, however, an important sign after coronary thrombosis. In the acute phase it is a manifestation of shock and has the appropriate prognostic significance, but it may remain subnormal for long periods after recovery. Acute infections of the heart such as in rheumatism and diphtheria, are associated with low blood pressure but a great reduction is only found when there is circulatory failure, when it depends as much upon peripheral as upon central factors. In mitral stenosis a blood pressure between 110 and 100 mm. Hg may be found and a similar level is sometimes noted during a paroxysm of tachycardia. It is therefore clear that low blood pressure should not be attributed to cardiac causes without definite evidence of structural disease.

PRIMARY LOW BLOOD PRESSURE

Primary low blood pressure is found in the absence of any of the organic diseases mentioned. Its incidence among healthy people has been estimated as between 3 and 4 per cent., and it is liable to occur in several members of a family. It is compatible with perfect health and well-being, but although it has been found in those of robust physique it is more commonly associated with people of slighter build, especially tall and thin "asthenics". Sometimes obvious signs of constitutional inferiority are present; poor muscular development, spinal lordosis, diminished chest expansion and a poor capacity for mental or physical effort. These people may have numerous complaints, such as exhaustion, nervousness, headaches, dizziness, dyspepsia, and constipation, and it is to them that the diagnostic label of "essential hypotension" has been applied. It is difficult to believe that low blood pressure can be the cause of such a diversity of symptoms, few of which are characteristic of circulatory

Washing out the colostomy.—This is a very satisfactory method of ensuring a bowel action in the morning, and for the rest of the day the patient will probably be free from the passage of faeces. The procedure is taught to the patient while he is in hospital and the following apparatus is provided: a douche receptacle, a length of rubber tubing and a soft rubber catheter of large bore.

To perform the wash-out the patient lies on his back with an inclination towards the left side and the lubricated catheter is inserted in the proximal loop of the colostomy for a distance of six inches. This must be done gently; no force is used on account of the risk of perforating the bowel. When the catheter is in position several ounces of a warm solution of soap and water are run in slowly; if this causes pain the stream is interrupted temporarily. Provided the flow is satisfactory and painless a quantity varying from half to one pint (284 to 568 c.cm.) of fluid is injected slowly. The patient begins to return the fluid at intervals into a bowl which is suitably placed to receive it. This procedure is carried out daily in the morning; at first the patient remains in bed but later it is advisable for him to be seated before the open toilet.

In some patients a natural action of the colostomy can be achieved, especially when a daily evacuation was the rule before operation. If an aperient is required liquid paraffin or milk of magnesia can be used. After several weeks the colostomy may be regulated satisfactorily by this method.

A patient with a colostomy should be reviewed at intervals in order to assess the condition for which the colostomy was instituted and, in addition, to examine the colostomy itself and evaluate its behaviour.

RONALD W. RAVEN, O.B.E., F.R.C.S.

LOW BLOOD PRESSURE

It is usual to consider as low a blood pressure with an arterial systolic level below 110 mm. of mercury, although some authorities prefer the figure of 100 mm. Hg. These standards are open to criticism since they discount to some extent the normal range of blood pressure variability and also alterations which may be expected with differences of age, sex, and race. There is, for instance, statistical evidence which suggests that below the age of sixteen the average systolic pressure in boys is 110 mm. Hg, and in girls 105 mm. Hg, whilst similar lowered pressures may be found in healthy adults in India and China. In contrast, it is well known that higher blood pressures are common after the age of forty-five and the formula of "age + 100 mm. of mercury" is generally accepted as giving normal levels. Some writers have applied the term "relative hypotension" to those cases in which the blood pressure remains normal with increase in age, but since there is little evidence to prove that any rise in blood pressure is physiological the term is unjustifiable. In view of these difficulties it seems wise, at least in adult Europeans, to restrict the term "low blood pressure" to an arbitrary level below 110 mm. Hg. Diastolic pressure has not been considered in this definition since it usually follows the systolic trend, unless it is lowered by itself as a result of some obvious abnormality such as aortic incompetence, or by an arteriovenous shunt.

Theoretically a low blood pressure may be expected whenever there is a failure of any factor responsible for maintenance of the normal level, the cardiac output, the peripheral resistance, or the blood volume; but in practice its cause is seldom clear-cut, since more than one factor is usually involved. Detailed consideration of this complex problem is beyond the scope of this article, but in general it may be said that "hypotension" is more often the result of peripheral than of central failure.

Clinical "low blood pressure" may be divided into two main groups, (1) primary, and (2) secondary.

SECONDARY LOW BLOOD PRESSURE

Secondary low blood pressure is found in a number of pathological states.

Acute circulatory failure characterized by low blood pressure with a rapid pulse

NOTES AND QUERIES

Laundering of Babies' Napkins

QUERY.—I should be grateful if you could advise me of a "safe" method for the laundering of babies' napkins. What is the effect of the use of soda in laundering processes on the production of napkin erythema?

REPLY.—The technique of washing babies' napkins used at this hospital is as follows:—

The soiled napkins are placed, without any unnecessary wringing, in bins, which are emptied into a washing machine, care being taken not to pack the napkins at all closely. The napkins are then subjected to half-an-hour's rinsing in cold running water; the water is then turned off and the napkins drained for ten minutes. A suitable amount of soap solution made from a good quality soap powder containing no free alkali is added, and steam is added to the washing machine and the contents boiled for twenty minutes. The soap solution is then drained off and replaced by hot water and boiling continued for ten or fifteen minutes. Finally, cold water is run through for a final rinse for half an hour. During all these processes the mechanical agitator is kept moving. Softened water is used. The end-result is a napkin free from any insoluble calcium or magnesium soap or alkali.

We have avoided using soda, but if both cold rinses are thoroughly carried out there should be no residual insoluble soap or soda left in the napkin, even if soda be used. On the other hand we found in the past that boiling with soda matted the fibres of the napkins and after a time made them harsh and liable to cause sore buttocks.

D. LANE (Matron),

W. W. PAYNE, M.B., B.S. (Biochemist).

The Hospital for Sick Children,

Great Ormond Street.

Duodenum Inversum

QUERY.—I have a female patient, aged seventy, who came to me complaining of various dyspeptic symptoms. The X-ray report shows it to be a case of duodenum inversum. As I can find no mention of this in my medical books and books of reference, I would be most obliged if you would let me know how common or rare the condition is, and in what book I can find any reference. I take it that the only thing for it is treatment of symptoms as they arise?

REPLY.—Reference to inverted duodenum can be found in "Gastro-enterology", by H. L. Bockus, vol. II, p. 49, and in Fieldman's "Clinical Roentgenology of the Digestive Tract", p. 417. In the former book it is stated that it is encountered in 0.07 per cent. of 20,000 gastro-enterological X-ray examinations. Fieldman doubts whether it is as rare as the literature would indicate. The condition predominates in the male sex and is not associated with any characteristic signs or symptoms. It may give rise to abdominal pain, nausea and a sense of fullness after meals, or symptoms suggestive of duodenal ulcer. It is most unwise to assume that it is the cause of symptoms unless more common causes have been excluded. This remark applies especially to the case in point, unless the patient has had indigestion for many years. The condition is a congenital developmental abnormality.

A. H. DOUTHWAITE, M.D., F.R.C.P.

Treatment of Napkin Erythema

QUERY.—I shall be obliged for information on the treatment of napkin erythema (Jacquet), with special reference to local applications.

REPLY.—The erythema of Jacquet is one type of napkin erythema. The condition is often due to irritation of the skin by alkali in the napkins, or especially to ammonia produced by bacterial fermentation of the urea in the urine, although some authorities believe there is a constitutional background to the complaint. I find the condition will usually respond quickly to grey powder, $\frac{1}{2}$ grain (16 mgm.) twice daily, and the application of the following paint to the affected area:—

R. Acriflavine	$\frac{1}{2}$ grain (32 mgm.)
Tannic acid	20 grains (1.3 gm.)
Water	to 1 ounce (28.4 c.cm.)

It is advisable to avoid strong alkalis and soap powders in washing the napkins, and after washing they may with advantage be rinsed in 1:2000 perchloride of mercury and then allowed to dry.

R. T. BRAIN, M.D., F.R.C.P.

Testicular Swelling and Pain

QUERY.—A patient aged thirty-eight years, three years married with no children, has for the past fifteen years had periodic pains in the scrotum accompanied by swelling in both testicles and the spermatic cords. The attacks occur every two to four weeks but recently have been getting more frequent. Relief is obtained only by cohabitation. There is no history of coitus interruptus, but the married life is not satisfactory. The patient complains of ejaculation before penetration takes place, and the wife remains unsatisfied. The patient was born with jaundice and there is a history of tuberculosis of the cervical glands and suspected tuberculosis of the kidney, also renal calculus for which no operation was performed. The family history is good. Examination of the patient at frequent intervals has verified the incidence and nature of the attacks. There is no evidence of recurrent epididymitis and testicular sensation is present and equal on both sides. The spermatic cords are thickened, but there is no prostatic enlargement or tenderness

failure, especially when it occurs as a symptomless abnormality in others who are either healthy or have recovered from a coronary thrombosis. It is more likely that both the symptoms and the lowered blood pressure are a result of the constitutional psychosomatic defect. Furthermore, a low blood pressure carries with it considerable immunity from degenerative cardiovascular disease and is a fortunate anomaly with unusually good prospects of long life. The diagnosis "essential hypotension" should therefore be discarded, since it suggests a false analogy with the serious condition of essential hypertension and gives unnecessary discredit to a sign of favourable import.

There remains for consideration *orthostatic hypotension* in which the presence of a low blood pressure is directly associated with the production of symptoms. In this condition the blood pressure, which is normal when the patient lies down, falls abruptly when he stands up. This may only be accompanied by negligible transient giddiness and vertigo, but on occasions there may be a larger fall (below 80 mm. Hg), which may lead to syncopal and even convulsive attacks. The symptoms sometimes appear only after the patient has stood for a few minutes, and always disappear when he lies down again. The essential disturbance is a failure of venous return and consequent fall in cardiac output due to pooling of blood in the lower limbs or in the abdomen. Vasomotor reflexes may be at fault, or there may be a loss of fluid from capillaries into the tissues when in the erect position.

Orthostatic hypotension may be latent, but susceptible people can be detected by means of the Flack test, in which artificial obstruction to the venous return, produced by blowing up a column of mercury to 30 mm. Hg for half a minute, causes failure of the radial pulse and fainting. The etiology of this malady is various: sometimes it occurs as a constitutional abnormality, usually in association with other signs of vasomotor defect, such as impaired sweating and cold extremities; at other times it seems to be caused by disease of the nervous system, such as neurosyphilis, subacute combined degeneration of the cord, or disseminated sclerosis. It is fairly common, too, after resection of the splanchnic sympathetic nerves for hypertension, but it can also be found as a transitory phenomenon in normal persons after prolonged periods in bed, and is probably responsible for some of the circulatory disorders of convalescence. Exercise and avoidance of the recumbent position help to correct orthostatic hypotension in the ordinary case, but in more persistent cases remarkable improvement can be obtained if the patient sleeps upright in bed with the head raised by 16 inches. Good results have also followed the use of sympathicomimetic drugs such as paredrine, and also by a diet rich in salt, which produces retention of fluid in the tissues which then appear to act as a splint for the capillary circulation.

CONCLUSION

The blood pressure is regarded as low when the arterial systolic pressure is below 110 mm. of mercury. It is an important sign in acute disorders of the peripheral circulation and an incidental finding in a number of organic diseases. Low blood pressure is also present in a small number of healthy people, some of whom are of inferior physique and complain of symptoms. These are probably not attributable to the low blood pressure and do not justify the diagnosis of "essential hypotension". The syndrome of "orthostatic hypotension" is, however, well established and promising methods of treatment have been described.

Low blood pressure is a clinical finding which may direct attention to the presence of organic disease, but by itself, unless orthostatic in nature, it does not deserve special notice either in diagnosis or treatment.

ALASTAIR HUNTER, M.D., F.R.C.P.

PRACTICAL NOTES

Poisoning Due to Ingestion of Wax Crayons

A CASE of poisoning after ingestion of wax crayons is recorded by E. B. Clark (*Journal of the American Medical Association*, December 6, 1947, 135, 917). The victim, a healthy boy of two years and four months, supposedly had a heart attack at his nursery school. There was intense cyanosis, black lips, and pulse of 140. Examination of the heart and lungs revealed no pathological reason for the child's condition, and poisoning with some methæmoglobin-producing substance was suspected. X-rays revealed a large amount of radio-opaque material in the stomach and intestines. Gastric lavage was carried out and large quantities of orange and yellow crayon obtained. Following lavage a dose of magnesium sulphate was administered. The child's condition was serious, and he was transferred to hospital where he was given an enema; more crayon, mostly orange, was obtained. Treatment in an oxygen tent, blood transfusion, and isotonic solution of sodium chloride produced improvement, and the following day the child was almost normal. Inquiries elicited the following facts:—On the day before being taken ill the child was known to have eaten most of an orange crayon; in the evening his colour was blue but he seemed normal. He was sent to school next morning but escaped routine inspection. At 10.30 a.m. a teacher noticed the child eating something and found he was just finishing a yellow crayon, part of which she scooped from his mouth. The cyanosis was noted and because of its intensity a heart attack was suspected; the eating of the crayon was not reported as it was considered to be harmless. The blood count was of interest as there was an initial and continued high white cell count and a somewhat persistent eosinophilia, which may have indicated some bone marrow irritation. A mild secondary anaemia developed nearly four weeks after the incident. As the case nearly proved fatal it constitutes a warning of the danger of coloured crayons containing aniline dye.

Antimony in Multiple Myeloma

BECAUSE antimony salts are of value in three diseases characterized by hyperglobulinæmia (kala-azar, lymphogranuloma venereum and schistosomiasis), M. A. Rubinstein (*Blood*, November 1947, 2, 555) decided to investigate its action in multiple myeloma, a condition in which there is also a marked hyperglobulinæmia. Tartar emetic was used originally, but proved to be too toxic. The antimonial preparation now

being used is neostibosan, which is given intravenously in divided doses of 0.3 gm. to a total dosage of 15 gm. In patients with renal involvement a careful watch must be kept on the urine and blood. Details are given of seven cases which have been treated and, whilst on the evidence available it is not possible to give a definite opinion as to the value of this form of treatment, it is claimed that the results "indicate a possible influence of antimony on myeloma tissue". The two main features in this small series of cases are that the antimonial appeared to give considerable relief of pain and that in some instances it appeared to increase the sensitivity of the myelomatous tissue so that a subsequent course of deep X-ray therapy produced a definite regression. It is of interest to note that Snapper (*Journal of Mount Sinai Hospital*, 1946, 13, 119) has claimed to obtain promising results in multiple myeloma with another drug that is effective in the treatment of schistosomiasis, namely stilbamidine, and that the basis of this form of treatment was also the hyperglobulinæmia common to the two conditions.

Antergan in the Treatment of Bronchial Asthma

THE results of a study of the value of the antihistamine drug "antergan" (dimethyl-aminoethyl - benzyl - anilin - dihydrochloride) in the treatment of bronchial asthma, carried out in a series of cases of one to thirty-six years' duration, are recorded by Th. Strengers, J. C. M. Verschure, and A. C. M. Lips (*Acta Medica Scandinavica*, 1947, 129, 193). Using Code's biological method the histamine level of the blood was first determined in all patients. In 17 of 46 cases investigated the blood histamine level was over 13 γ /100 c.cm. Twenty-three cases were selected for antergan therapy, the drug being given either orally, in 0.1 gm. tablets, 6 daily at equal intervals, or by intramuscular injection using ampoules containing 0.05 gm. antergan. The dosage was decreased by 2 tablets after four days and again at further four-day intervals. Food was always given at the time of antergan administration. Of the 23 patients treated, 8 responded well, 6 fairly well, in 5 there was no improvement, and in 4 initial improvement was followed by relapse. Ten of the patients had an initial raised histamine level in the blood, and in all definite improvement was noted after antergan therapy. Of 12 with initial normal blood histamine levels, 4 showed definite improvement, 2 moderate, and in 6 the initial improvement was followed by relapse. Slight secondary reactions were noted in 5 of the 23

on rectal examination. Examination of the urine is negative for deposits, bacteria, albumin and sugar; there is a slightly acid reaction. Wassermann test negative. Central nervous system, heart, lungs and other organs normal.

REPLY.—According to the report of the clinical examination there is nothing to suggest that the periodic swelling and pain in the testicles are due to recurrent attacks of epididymitis, and there is no evidence of urinary infection. There is only one other cause of attacks of testicular swelling and pain, namely, congestion of the genital tract. These attacks are generally due to strong sexual stimulation unfulfilled by gratification. Long engagements are often responsible for them and they disappear with marriage. In this case the unsatisfactory sexual life certainly accounts for the pain. Premature ejaculation is very difficult to treat and it is often psychogenic. In this case it is almost certainly psychological in origin and will only yield to expert psychotherapy. The patient should therefore be put into the hands of the best psychologist available. It has been said that the use of coitus interruptus as a method of birth control can give rise to this condition, but it is not often due to such a cause.

KENNETH WALKER, F.R.C.S.

Treatment of Giant Urticaria

QUERY.—I should be grateful for any information you can give me concerning the modern treatment of angioneurotic oedema (Quincke). For the past two months I have had a male patient, aged thirty-three, under my care for this condition. For fourteen months he has been having daily urticaria-like eruptions, which usually appear in the evening. These may last a matter of minutes or hours and involve any part of the body. At various times I have given him phrenazol, bellergal, nicotamide and intra-dermal milk injections, but without success.

REPLY.—Treatment directed at possible causes may be effective in cases in which such factors can be identified. When a specific food allergy is suspected removal of the food from the diet may result in recovery. When attacks occur at frequent intervals, however, the tracing of food allergy is more difficult and careful elimination diets are usually needed. Achlorhydria and hyperchlorhydria should be looked for, and if present treated. Focal sepsis in the teeth or upper respiratory tract is present in a proportion of cases; its removal sometimes results in cure. Overwork, worry and anxiety form the basis of some cases and indicate the obvious remedy.

Among non-specific measures, autohæmotherapy often gives good results, consisting of injections of 3 to 10 c.cm. of whole blood every five to seven days. Calcium is preferred by some; it may be given as the lactate by the mouth but is more likely to succeed when given by injection, either as the chloride intravenously or as the gluconate intramuscularly. Anti-allergic drugs such as benadryl and antistine often prevent attacks when given by the mouth in doses of 50 to 100 mgm., three or four times a day. Their effect is liable to last only so long as dosage is maintained, but treatment continued over many weeks appears to be free from danger. During the attacks cold compresses applied to the affected areas give some relief. Oedema of the tongue, pharynx or larynx may be an alarming and dangerous feature. The prompt injection of adrenaline (1:1000), $\frac{1}{2}$ to 1 c.cm. subcutaneously, will usually bring speedy relief, but occasionally tracheotomy is necessary to save life.

F. RAY BETTLEY, M.D., M.R.C.P.

Birth Control

QUERY.—I shall be pleased if you will advise me as to the best method of birth control for a young intelligent couple about to be married, who do not desire to have a family for a year or so.

REPLY.—The only reliable contraceptive method is a barrier plus an adequate chemical. The barrier can take the form of a sheath used by the man, the chemical being used by the woman, or both barrier and chemical being used by the woman. The latter, if provided under expert medical supervision should give a 98 per cent. safety margin. Various opinions exist regarding the use of contraceptives at the marriage onset; some consider it inadvisable to use anything, others recommend the man to use a sheath and possibly the woman to use a chemical. Others again recommend the preliminary dilatation of the hymen by a doctor or the patient and the fitting of a cap, the most commonly used being the diaphragm. The latter method is most reliable and should be possible in all cases. It ensures easy penetration, enables the couple to achieve adequate emotional release before embarking on a pregnancy, and enables the physician to give the couple, or at any rate the woman, considerable premarital help concerning the psychological and technical aspects of marriage. Diaphragm caps are most generally used, are easier to manage, and two excellent chemicals are Volpar paste and G.P. ointment.

EDWARD F. GRIFFITH, M.R.C.S., L.R.C.P.

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being used is neostibosan, which is given intravenously in divided doses of 0.3 gm. to a total dosage of 15 gm. In patients with renal involvement a careful watch must be kept on the urine and blood. Details are given of seven cases which have been treated and, whilst on the evidence available it is not possible to give a definite opinion as to the value of this form of treatment, it is claimed that the results "indicate a possible influence of antimony on myeloma tissue". The two main features in this small series of cases are that the antimonial appeared to give considerable relief of pain and that in some instances it appeared to increase the sensitivity of the myelomatous tissue so that a subsequent course of deep X-ray therapy produced a definite regression. It is of interest to note that Snapper (*Journal of Mount Sinai Hospital*, 1946, 13, 119) has claimed to obtain promising results in multiple myeloma with another drug that is effective in the treatment of schistosomiasis, namely stilbamidine, and that the basis of this form of treatment was also the hyperglobulinæmia common to the two conditions.

Antergan in the Treatment of Bronchial Asthma

THE results of a study of the value of the antihistamine drug "antergan" (dimethyl-amino-ethyl-benzyl-anilin-dihydrochloride) in the treatment of bronchial asthma, carried out in a series of cases of one to thirty-six years' duration, are recorded by Th. Strengers, J. C. M. Verschure, and A. C. M. Lips (*Acta Medica Scandinavica*, 1947, 129, 193). Using Code's biological method the histamine level of the blood was first determined in all patients. In 17 of 46 cases investigated the blood histamine level was over 137/100 c.cm. Twenty-three cases were selected for antergan therapy, the drug being given either orally, in 0.1 gm. tablets, 6 daily at equal intervals, or by intramuscular injection using ampoules containing 0.05 gm. antergan. The dosage was decreased by 2 tablets after four days and again at further four-day intervals. Food was always given at the time of antergan administration. Of the 23 patients treated, 8 responded well, 6 fairly well, in 5 there was no improvement, and in 4 initial improvement was followed by relapse. Ten of the patients had an initial raised histamine level in the blood, and in all definite improvement was noted after antergan therapy. Of 12 with initial normal blood histamine levels, 4 showed definite improvement, 2 moderate, and in 6 the initial improvement was followed by relapse. Slight secondary reactions were noted in 5 of the 23

on rectal examination. Examination of the urine is negative for deposits, bacteria, albumin and sugar; there is a slightly acid reaction. Wassermann test negative. Central nervous system, heart, lungs and other organs normal.

REPLY.—According to the report of the clinical examination there is nothing to suggest that the periodic swelling and pain in the testicles are due to recurrent attacks of epididymitis, and there is no evidence of urinary infection. There is only one other cause of attacks of testicular swelling and pain, namely, congestion of the genital tract. These attacks are generally due to strong sexual stimulation unfollowed by gratification. Long engagements are often responsible for them and they disappear with marriage. In this case the unsatisfactory sexual life certainly accounts for the pain. Premature ejaculation is very difficult to treat and it is often psychogenic. In this case it is almost certainly psychological in origin and will only yield to expert psychotherapy. The patient should therefore be put into the hands of the best psychologist available. It has been said that the use of coitus interruptus as a method of birth control can give rise to this condition, but it is not often due to such a cause.

KENNETH WALKER, F.R.C.S.

Treatment of Giant Urticaria

QUERY.—I should be grateful for any information you can give me concerning the modern treatment of angioneurotic oedema (Quincke). For the past two months I have had a male patient, aged thirty-three, under my care for this condition. For fourteen months he has been having daily urticaria-like eruptions, which usually appear in the evening. These may last a matter of minutes or hours and involve any part of the body. At various times I have given him phrenazol, bellergal, nicotamide and intradermal milk injections, but without success.

REPLY.—Treatment directed at possible causes may be effective in cases in which such factors can be identified. When a specific food allergy is suspected removal of the food from the diet may result in recovery. When attacks occur at frequent intervals, however, the tracing of food allergy is more difficult and careful elimination diets are usually needed. Achlorhydria and hyperchlorhydria should be looked for, and if present treated. Focal sepsis in the teeth or upper respiratory tract is present in a proportion of cases; its removal sometimes results in cure. Overwork, worry and anxiety form the basis of some cases and indicate the obvious remedy.

Among non-specific measures, autohæmotherapy often gives good results, consisting of injections of 3 to 10 c.cm. of whole blood every five to seven days. Calcium is preferred by some; it may be given as the lactate by the mouth but is more likely to succeed when given by injection, either as the chloride intravenously or as the gluconate intramuscularly. Anti-allergic drugs such as benadryl and antistine often prevent attacks when given by the mouth in doses of 50 to 100 mgm., three or four times a day. Their effect is liable to last only so long as dosage is maintained, but treatment continued over many weeks appears to be free from danger. During the attacks cold compresses applied to the affected areas give some relief. Oedema of the tongue, pharynx or larynx may be an alarming and dangerous feature. The prompt injection of adrenaline (1:1000), $\frac{1}{2}$ to 1 c.cm. subcutaneously, will usually bring speedy relief, but occasionally tracheotomy is necessary to save life.

F. RAY BETTLEY, M.D., M.R.C.P.

Birth Control

QUERY.—I shall be pleased if you will advise me as to the best method of birth control for a young intelligent couple about to be married, who do not desire to have a family for a year or so.

REPLY.—The only reliable contraceptive method is a barrier plus an adequate chemical. The barrier can take the form of a sheath used by the man, the chemical being used by the woman, or both barrier and chemical being used by the woman. The latter, if provided under expert medical supervision should give a 98 per cent. safety margin. Various opinions exist regarding the use of contraceptives at the marriage onset; some consider it inadvisable to use anything, others recommend the man to use a sheath and possibly the woman to use a chemical. Others again recommend the preliminary dilatation of the hymen by a doctor or the patient and the fitting of a cap, the most commonly used being the diaphragm. The latter method is most reliable and should be possible in all cases. It ensures easy penetration, enables the couple to achieve adequate emotional release before embarking on a pregnancy, and enables the physician to give the couple, or at any rate the woman, considerable premarital help concerning the psychological and technical aspects of marriage. Diaphragm caps are most generally used, are easier to manage, and two excellent chemicals are Volpar paste and G.P. ointment.

EDWARD F. GRIFFITH, M.R.C.S., L.R.C.P.

Stephens et al. (*Annals of Internal Medicine*, September 1947, 27, 420) investigated the action of folic acid in twenty patients with rheumatoid arthritis. Ten patients received 5 mgm. of folic acid by mouth four times daily; the remainder received the same dose of folic acid plus ferrous salts by mouth. Seven patients failed to respond to this dosage, but when the daily intake of folic acid was increased to 100 mgm. daily there was a satisfactory response, so that in the end there was a response in every patient. This response consisted of "an increase in the mean corpuscular volume, the hematocrit, the hæmoglobin, the colour index, and the morphology of the erythrocytes without comparable rise in the total erythrocyte or leucocyte counts". Although the administration of iron had no apparent effect in these patients, it is pointed out that in some patients with rheumatoid arthritis there is undoubtedly a deficiency of iron and that in such patients iron will be required in addition to folic acid. It is stressed that the administration of folic acid had no apparent effect upon the rheumatoid arthritis. The dose of folic acid required to produce an effect upon the blood picture varied considerably in different patients.

Tetraethyl Ammonium Bromide in Hypertension and Hypertensive Heart Failure

THE results of an investigation undertaken to determine the value of administration of tetraethyl ammonium bromide (T.E.A.B.) as a preoperative test in the selection of hypertensive patients for sympathectomy are recorded by G. W. Hayward (*Lancet*, January 3, 1948, i, 18). The drug was given intravenously in a 10 per cent. solution, in doses of 0.3 to 0.5 gm. (4 to 6 mgm. per kg. body weight), the injection being given slowly and the patient kept in the recumbent position for 30 to 40 minutes after injection. The average blood pressure after T.E.A.B. administration was 58 mm. Hg systolic and 28 mm. Hg diastolic; with sodium amylal, the results of the administration of which were compared with those obtained with T.E.A.B., the fall in systolic pressure was 74 mm. Hg and diastolic 35 mm. Hg. No toxic effects of T.E.A.B. were noted: the blood pressure remained low for 5 to 30 minutes after intravenous injection, and for 2 to 8 hours after intramuscular injection. A comparison of the preoperative blood pressures after injection of T.E.A.B. and after administration of sodium amylal, with those registered two weeks after transthoracic splanchnic neurectomy in ten patients, showed that the T.E.A.B. preoperative

test blood pressures agreed within 10 mm. Hg with the postoperative levels in seven cases out of ten, compared with nine cases out of ten with sodium amylal. The administration of T.E.A.B. to patients with hypertensive heart failure resulted in temporary relief of orthopnoea and dyspnoea. It is stated that the drug may be useful in the emergency treatment of acute left ventricular failure, but owing to the fall in urinary output which follows the lowering of blood pressure its use is inadvisable in the treatment of patients with chronic congestive failure.

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Two preparations for use in the treatment of chapped hands and lips are given by J. G. Downing (*New England Journal of Medicine*, November 20, 1947, 237, 755). For the hands:—

R	Tincture of benzoin	15 c.cm.
	Glycerol	10 c.cm.
	Rose water (as needed) to make a solution of	250 c.cm.

For chapped and fissured lips:—

R	Sodium borate	6 gm.
	Tincture of myrrh	20 c.cm.
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When the skin becomes crusted, bathing with equal parts of a 2 per cent. solution of boracic acid and a 10 per cent. solution of aluminium acetate is advocated until the crusts soften and become detached (they should never be removed forcibly), when a zinc oxide paste, or one containing glycerin, should be applied.

Dirty Dish Washing

AN interesting sidelight on the efficacy of methods of dish washing is revealed by a survey of dish washing procedures in 1,005 restaurants in New York City reported on by H. J. Kleinfeld and L. Buchbinder in the *American Journal of Public Health* (April 1947, 37, 379) and summarized in *The Laboratory Digest* (July 1947, II, 12). About 88 per cent. of the establishments used hand methods entirely or in part, and only 17.5 per cent. used machine methods entirely or in part. "The quality of washing as measured by the swab-rinse test was found in general to be very poor". Thus, in the case of hand-washed glasses and cups only 176 out of 1,675 samples (10.5 per cent.) passed the test; the comparable figures for machine-washed ones were 509 out of 1,421 samples (35.8 per cent.). In the case of spoons and forks, 509 out of 1,421 hand-washed samples (35.8 per cent.) came up to standard, whilst for machine-washed ones the comparable figures were 89 out of 251 samples (35.4 per cent.).

cases—gastric pain, nausea, fatigue, headache and vertigo—but in no instance were the symptoms severe enough to interfere with continuation of the treatment. The use of antergan in the treatment of asthma with raised blood histamine levels is stressed by the authors.

Lymphocytes and Immunity

ACCORDING to O. A. Trowell (*Nature*, December 13, 1947, 160, 845) recent American work suggests that an important function of the lymphocytes is the synthesis, and subsequent liberation into the blood, of the normal γ -globulin of the plasma and the various antibodies which appear in the blood in immunity reactions. About 200 million lymphocytes per hour enter the blood stream. They are removed by a process of "dissolution" in the germinal centres of the lymph nodes. In this process of dissolution, γ -globulin is liberated and carried away in the lymph stream to the blood. The antibodies of the blood are known to be specific modifications of normal plasma γ -globulin, and it is thought that in an immunity reaction the lymphocytes manufacture the specific antibody in place of the normal γ -globulin. It has also been shown that the adrenal cortical hormone stimulates the dissolution of lymphocytes in the germinal centres and so increases the liberation of γ -globulin and antibodies in the blood. Experiments have shown that if an animal is immunized to an antigen and then some months later, when all the antibody has disappeared from the blood, it is injected with adrenal cortical hormone, the antibody reappears in the blood. A further observation is that the total amount of lymphoid tissue in the body is determined and controlled by the adrenal cortex.

Joll's Linctus for Bronchial Cough

A MODIFIED prescription of Joll's linctus, which he used with success for the removal of tenacious sputum in postoperative cases, is advocated for the treatment of chest cases with thick bronchial secretion by W. H. Myers (*Pharmaceutical Journal*, December 6, 1947, 159, 413):—

R Morphine sulphate	‡ grain (32 mgm.)
Atropine sulphate	1/100 grain (0.65 mgm.)
Apomorphine hydrochloride	1/12 grain (5.4 mgm.)
Dilute hydrochloric acid ..	40 minims (2.4 c.cm.)
Solution of Bordeaux B ..	5 minims (0.3 c.cm.)

Syrup of tolu
Chloroform water equal
parts to 1 fluid ounce (28.4 c.cm.)
Dose: 1 teaspoonful four times daily.

The syrup of tolu is substituted for syrup of lemon, which is difficult to obtain at the present time, the hydrochloric acid to retard the action of oxygen and light on the apomorphine, and solution of Bordeaux as a permanent colour-

ing substance. It is stated that the mixture is in every way as efficacious as the original: the pair of the hard cough is relieved by the apomorphine which also acts as an expectorant, and the spasm of the bronchioles is relaxed by the atrophine. The mixture is made palatable by the addition of syrup of tolu and chloroform water and pleasing to the eye by addition of the colouring matter.

Ingestion of Amphetamine Sulphate (Benzedrine) from Inhalers

THE growing practice of ingestion of the volatile base of benzedrine inhalers as a stimulant is stressed by R. R. Monroe and H. J. Dr. (*Journal of the American Medical Association* December 6, 1947, 135, 909), who record the results of an investigation carried out in United States military prison, where it was found that the ingestion of the volatile base of amphetamine inhalers had led to serious disciplinary, medical and psychiatric problems: 25 per cent. of the inmates of the prison were found to have used the inhalers in this manner and 14 per cent. admitted having so taken the base in civilian life. Acute abdominal symptoms, hallucinations, psychotic symptoms and personality changes were recorded, and the fact that withdrawal of the drug precipitated weakness, depression, gastro-intestinal disturbance and tremor was evidence of addiction. It is stated that this misuse of inhalers is not by any means limited to inmates of military prisons: although the practice was prevalent among military personnel on active service, doubtless because of the "pep" resulting from ingestion of the drug. The report concerns benzedrine inhalers N.N.R. which are issued in a plastic case bearing the warning "for inhalation only unfit for internal use—dangerous if swallowed". The warning apparently does not act as a deterrent. Inside the plastic case is a paper folded into 8 sections, each of which contains approximately 31 mgm. of the amine base, the total contents of the case representing 250 mg of synthetic racemic amphetamine base (but phenylisopropylamine), 12.5 mgm. menthol aromatics. It is pointed out that a number of other similar inhalers are appearing on the market, and the advisability of the development of an inhaler containing a volatile local vasoconstrictor which would be inactivated or absorbed in the gastro-intestinal tract is emphasized.

Folic Acid in the Anæmia of Rheumatoid Arthritis

BECAUSE of the poor response of the anæmic rheumatoid arthritis to iron or liver, C. A.

Stephens *et al.* (*Annals of Internal Medicine*, September 1947, 27, 420) investigated the action of folic acid in twenty patients with rheumatoid arthritis. Ten patients received 5 mgm. of folic acid by mouth four times daily; the remainder received the same dose of folic acid plus ferrous salts by mouth. Seven patients failed to respond to this dosage, but when the daily intake of folic acid was increased to 100 mgm. daily there was a satisfactory response, so that in the end there was a response in every patient. This response consisted of "an increase in the mean corpuscular volume, the hematocrit, the hemoglobin, the colour index, and the morphology of the erythrocytes without comparable rise in the total erythrocyte or leucocyte counts". Although the administration of iron had no apparent effect in these patients, it is pointed out that in some patients with rheumatoid arthritis there is undoubtedly a deficiency of iron and that in such patients iron will be required in addition to folic acid. It is stressed that the administration of folic acid had no apparent effect upon the rheumatoid arthritis. The dose of folic acid required to produce an effect upon the blood picture varied considerably in different patients.

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REVIEWS OF BOOKS

Good Health with Diabetes. BY IAN MURRAY, M.D., F.R.F.P.S.G., F.R.C.P. Ed., and MARGARET B. MUIR, S.R.N. Edinburgh: E. & S. Livingstone Ltd., 1947. Pp. 40. Price 2s.

THIS admirable little book is to be thoroughly recommended for the use of patients with diabetes mellitus. In it they will find a brief practical description of how to cope with their diets and the administration of insulin. It also summarizes the salient features of hypoglycæmia and outlines the measures to be taken in dealing with this complication as well as "emergencies" such as febrile illnesses, sore feet and diabetic coma. Practitioners will find it most valuable in supervising their diabetic patients, whilst the patients themselves will find in it the answer to most of those questions which vex the diabetic until he becomes used to his new mode of life. In subsequent editions more emphasis should be laid upon the necessity for ensuring that the needle and syringe do not contain any spirit before inserting the needle into the vial of insulin.

The Parathyroid Glands and Skeleton in Renal Disease. BY J. R. GILMOUR. London: Oxford University Press, 1947. Pp. xiii and 157. Figures 26. Price 18s.

ALTHOUGH the association of renal disease with changes in the parathyroids and the bony skeleton has long been recognized, this would appear to be the first monograph on the subject. The author is mainly concerned with the histological aspect, and the chemical side of the condition is only briefly dealt with, although it is concluded that the hypocalcæmia resulting from phosphate retention is the immediate stimulus to the parathyroid hyperplasia, which might therefore be regarded as compensatory. The osteitis fibrosa resulting in the adult is described, and a full account is given of the bony changes in eight cases of renal rickets, some active and some healed. Both osseous and parathyroid changes are admirably illustrated. The book is essentially intended for the specialist, and not for the practitioner. It obviously represents the fruit of much meticulously careful work, and maintains the high standard of the Institute from which it originates.

The Occasion Fleeting. BY HUGH BARBER, F.R.C.P. London: H. K. Lewis & Co. Ltd., 1947. Pp. 199. Price 15s.

THIS delightful volume of essays by a distinguished son of Guy's will appeal to many

generations of readers. To the author's contemporaries it will recall memories of those spacious Edwardian days when a man was what he proved to be, and not what a dominating State decreed he should be. To the post-1918 generation it will conjure up visions of a mellow and gracious era which would have been balm to the restless soul of the between-war period. To the generation of to-day it will come as a revelation of the leisurely age in which their grandparents were privileged to live. Above all it can be recommended as a bedside book for the young practitioner who wishes to serve his patients well. For here he will find how to deal with "patients" as opposed to "cases". Here he will find the chapters headed "clinical acumen", "the spirit of the family doctor", "the relatives and friends". And if he is wise he will ponder carefully the words of this wise physician, for in them, and not in the abstruse technology of the laboratory, lies the secret of success for both practitioner and patient.

Progress in Gynecology. Edited by J. V. MEIGS, M.D., and S. H. STURGIS, M.D. London: William Heinemann (Medical Books) Ltd., 1947. Pp. xiii and 552. Figures 67. Price 35s.

THE contributors to this volume range from Aldridge to Venning, Watson, and Williams; the eminent in gynecology and allied subjects over the North American continent. Their aim has been to give an account of recent work and each contributor has written on the subjects of his own interest. The aim has been achieved. Most aspects of gynecology have been covered from embryology, physiology and anatomy, to the main clinical advances. Thus is rendered available to the general medical reader in one book the main work of recent years, and the specialist is provided with the "high lights" from which further exploration may easily be made. The book is well produced and worthy of purchase. Like much American literature nearly all references are to American work. This speaks well of the vitality of American gynecology, but a better balance might be preserved if British and Continental references were included more freely when merited.

Pharmakologie. BY K. O. MOLLER, Basle: Benno Schwabe & Co., 1947. Pp. 744. Figures 54. Price. Sw. frs. 48.

THIS is a translation into German by Dr. O. Walker of the revised edition of a book first published in Danish in 1941. The emphasis

throughout is on drugs in common use and the section on chemotherapeutic agents is a model of effective condensation. The revision is fully up to date and short accounts of tyrothricin, streptomycin, propamidine, phenoxetol and paludrine are included in this section. Indeed almost all the drugs of proved value recently introduced into medicine receive mention; folic acid and the antihistamine group of substances which are not discussed in the book have not yet a fully defined place in treatment. An admirably critical outlook is preserved throughout. The clinician will find refreshment on almost every page. The pharmacologist will be especially interested in the attention given to work carried out during the war period in the Scandinavian countries and in particular in Denmark itself. The large number of references to papers published in many countries helps to correct the impression sometimes created in recent textbooks that little work of merit has been carried out except in the United States of America. The index is adequate. Altogether this book can be highly recommended.

Malaria: With Special Reference to the African Forms. By W. K. BLACKIE, M.D., Ph.D., F.R.C.P.Ed., D.T.M. & H. Cape Town: The African Bookman; Post-Graduate Press, 1947. Pp. 101.

WELL written, well arranged and easy to read, this little book has much to recommend it. In a book of this size a shorter general account of the morbid anatomy would have been adequate. The author takes the view that one of the primary factors in the production of the clinical pattern is the anatomical site of massive internal parasitization. This is not in keeping with the modern view, which is that selective concentration of parasites in organs does not necessarily play an important part in the production of clinical symptoms; it is not a significant feature, for instance, in cerebral malaria. The clinical portion of the book is well done. The section on drug treatment is clear and practical. It is difficult, however, to interpret the author's views concerning intravenous injection of mepacrine and the combination of this form of therapy with intramuscular injection. The reviewer, in common with most others who have worked extensively with mepacrine, takes the view that intravenous injection of mepacrine should be avoided on account of its toxic effects.

NEW EDITIONS

Short Textbook of Surgery, by C. F. W. Illingworth, C.B.E., M.D., CH.M., F.R.C.S.Ed., in its fourth edition (J. & A. Churchill Ltd., 30s.)

contains a wealth of new material. The advent of penicillin, the anticoagulants, protein hydrolysates and thiouracil has revolutionized many branches of surgery. The inclusion of these and other advances, and new sections on arterial injuries, dysphagia, reticulosarcoma, and rehabilitation, makes the new edition of this well-known textbook a valuable addition to the surgeon's library.

THE use of protein hydrolysates in malnutrition, folic acid in macrocytic anæmias and sprue, benadryl and pyribenzamine in allergic disorders, thiouracil in hyperthyroidism, and penicillin in syphilis and infections are among the therapeutic measures included in *Internal Medicine in General Practice*, by Robert Pratt McCombs, M.D., B.S., F.A.C.P., in its second edition (W. B. Saunders Co., Ltd., 42s.). A new chapter on psychiatric disorders has been added, and in the chapter on vascular disturbances a section is devoted to anticoagulant therapy.

THE fourth edition of *The Treatment of Rheumatism in General Practice*, by W. S. C. Copeman, O.B.E., M.D., F.R.C.P. (Edward Arnold & Co., 12s. 6d.), presents the methods of treatment of rheumatism in its many aspects and concludes with a chapter on prognosis and end-results. A useful addition to the practitioner's library.

IN the preparation of the fourth edition of *Gifford's Textbook of Ophthalmology*, by Francis H. Adler, M.D. (W. B. Saunders Company, 30s.) the original purpose of the book has been adhered to, i.e., to provide medical students and practitioners with a guide to the diagnosis and treatment of those ophthalmic conditions met with in daily medical practice. The new edition is well produced and illustrated.

Illustrations of Regional Anatomy, by E. B. Jamieson, M.D., in its seventh edition (E. & S. Livingstone Ltd., in one volume 75s., or in separate sections). Some alterations to the illustrations and additions to the pointer legends bring this well-known aid to the study of anatomy to a high level of perfection.

Year Book of Pediatrics, 1947, edited by Isaac A. Abt, M.D. (Year Book Publishers, Chicago; H. K. Lewis & Co., 21s.), contains among the many new additions sections on the use of benadryl and the antihistamine drugs in allergy, the development and use of BAL in the treatment of arsenical dermatitis, and the X-ray evidence of changes in the lungs of B.C.G. vaccinated children.

NOTES AND PREPARATIONS

NEW PREPARATION

PENTAMIDINE ISETHIONATE—M & B (4:4' diaminodiphenoxypentane di-(β -hydroxyethanesulphonate), an aromatic diamidine compound, is claimed to be effective in the treatment of kala-azar, trypanosomiasis and leishmaniasis. In order to obviate the systemic reactions which commonly result from the administration of the aromatic diamidines, pentamidine isethionate should be given by intramuscular route. It is supplied in powdered form, in boxes of 10 and 50 ampoules of 200 mgm. and also in multidose containers of 2 gm., by May & Baker Ltd., Dagenham, Essex, from whom literature can be obtained.

The manufacturers are Homeware Co. (Hook) Ltd., Hook, Surbiton, Surrey. Price 30s. with out hosepipe.

PUBLISHERS' ANNOUNCEMENTS

THE opening of a London branch of the firm of E. & S. Livingstone Ltd. of Edinburgh, at 4 Lincolns Inn Fields, W.C.2, is announced. An invitation to pay a visit to the new branch is extended to practitioners.

Mr. John Maitland, Assistant Medical Editor at the Oxford University Press, has been appointed Joint Managing Editor (with Dr. Maurice Newfield) of Hamish Hamilton Medical Books Ltd.

PUBLICATIONS

Antenatal and Postnatal Exercises gives two schemes of exercises with accompanying illustrations, one for prenatal and the other for postnatal use. Copies of the pamphlet, price 1d. can be obtained from the secretary, National Baby Welfare Council, 29 Gordon Square London, W.C.1.

The Cord is the journal of the paraplegic branch of the British Legion. This branch of the Legion was formed in June, 1947, with the object of spreading information of particular interest to paraplegics and of fostering in civilian life the spirit of comradeship which grew up in the Services and in hospital. The journal is published quarterly, and the first issue, which appeared in the autumn of 1947, contains among other items: a message from Sir Brunel Cohen, Chairman of the Committee, an account of Sir Ian Fraser's visit to Stoke Mandeville, during which he made the suggestion for the formation of the paraplegic branch, and an account of "Chaseley", Eastbourne, the hospital for paraplegic ex-Servicemen. *The Cord* is published by the Paraplegic Branch of the British Legion, Stoke Mandeville Hospital, Aylesbury, Bucks, price 2s. p.a.

Medical Bookman and Historian (Harvey & Blythe Ltd., 6 Hanover Square, W.1, monthly, 2s.; 25s. p.a.) starting its second year, now includes a historical supplement. This enterprising venture can be recommended for its authoritative, well-written reviews, its pleasant bypaths, and its agreeable typography.

Ninety-Nine, incorporating "Doctor" (15 & 16 City Road, E.C.1, monthly 1s.; 13s. 6d. p.a.), intended for the lay public, could well find a place in the doctor's waiting-room. Elegantly produced, its articles are lucidly, soberly, and attractively written, and well illustrated.

The contents of the March issue, which will contain a symposium on "Orthopaedics in General Practice", will be found on page lxiv at the end of the advertisement section.

THE ROWLEY BRISTOW ORTHOPÆDIC HOSPITAL

THIS is the new name which the Committee of the Waifs and Strays, now called the Church of England Children's Society, has decided to adopt for the formerly known St. Nicholas' and St. Martin's Hospital for Crippled Children. The renaming of the Hospital is a tribute to the late Mr. Rowley Bristow in appreciation of his long and brilliant services to the Hospital.

DIRECTORY OF CONVALESCENT HOMES

THE "Directory of Convalescent Homes", issued by the Convalescent Homes Committee of King Edward's Hospital Fund, gives information concerning Convalescent Homes within the four London regions and those Homes outside the regions which take patients from London. Homes for all types of patients are included, and a special index has been compiled to facilitate easy reference. This directory, which is well produced, and bound in loose-leaf form so that further additions may be made, will be much appreciated by practitioners. It is obtainable from George Barber & Son Ltd., Furnival Street, London, E.C.4, at an initial fee of 5s., which entitles subscribers to all additional pages and amendments until January 1, 1950.

A CAR WASHER

THE "Torant" car washer is fitted with a specially constructed handle which, when attached to a $\frac{1}{2}$ in. of $\frac{3}{8}$ in. hosepipe allows the water to flow to the mop-like head and spray from the fabric. A "jet-cap" is supplied as a substitute for the mop when cleaning the undercarriage and wings. Among the advantages claimed for the "Torant" washer are the speed of cleaning, the softness of the mop so that the most delicate surface is not injured, and the safety from splashing of the operator's clothes.

THE AFTER-TREATMENT OF ANTERIOR POLIOMYELITIS

By H. J. SEDDON, D.M., F.R.C.S.

Nuffield Professor of Orthopædic Surgery, University of Oxford.

A SURGEON called upon to deal with patients suffering from poliomyelitis will be faced with an important question of hospital policy; if the disease is epidemic the answer is of paramount importance. Should a patient suffering from poliomyelitis, or suspected to be suffering from it, be admitted in the initial stage to a fever hospital or to an orthopædic hospital? It is generally agreed that the responsibilities of the orthopædic surgeon begin as soon as paralysis is present, and for this reason many favour immediate admission to an orthopædic hospital. There are, however, certain practical objections. The suspected case may be found after all to be suffering from some other condition, such as meningitis or rheumatic fever; an efficient fever hospital is in a better position to treat or place cases of this kind. In established poliomyelitis, barrier nursing is desirable for a period of about three weeks. In fever hospitals such measures are common form; in orthopædic hospitals they are not, and the structure of the hospital is often unfavourable for efficient isolation. Lastly, there are the cases in which no paralysis develops or in which it is transitory: they require supervision but no orthopædic treatment. Orthopædic hospitals throughout the country have long waiting lists; to admit all cases of poliomyelitis to them would be at the unnecessary expense of patients whose need of treatment is unquestioned. For all these reasons therefore the most sensible plan is first to admit poliomyelitis patients to a fever hospital on the clear understanding that they are seen at the earliest possible moment by an orthopædic surgeon, and that adequate provision is made for such treatment as he deems necessary. Ideally, the orthopædic hospital and fever hospital should be fairly close to each other, for the surgeon will not have time to travel widely to see cases as they arise and to follow their progress regularly during the early weeks of the illness. It is desirable for the fever hospitals in an area to come to an arrangement whereby all cases of poliomyelitis, overt or suspected, are admitted to the fever hospital nearest to the orthopædic centre. This should be done even if it means sending patients suffering from other infectious diseases to outlying fever hospitals in order to free beds at the central hospital for cases of poliomyelitis. A scheme of this kind was applied in the Oxford region during the 1947 epidemic and, although there was a shortage of beds at the central fever hospital, the organization was, on the whole, satisfactory.

Cases requiring prolonged treatment are transferred to the orthopaedic hospital in due course.

SOME FEATURES OF THE DISEASE

A rational plan for the treatment of paralytic poliomyelitis must be based on knowledge of the pathology of the disease and of the natural process of recovery. The difficulty is that there are still extensive gaps in our knowledge, with the result that there is still a lack of uniformity in methods of treatment.

Changes in the nervous system.—It is common knowledge that anterior horn cells are often completely destroyed, sometimes on a large scale. Their axons degenerate, and the muscles they supply are completely and permanently paralysed. On the other hand, the neuronal damage may be comparatively mild, with no axonal degeneration and therefore no significant structural change in the affected muscles. In such cases recovery occurs within a few weeks or months. The important question is whether there is an intermediate group in which, as a result of moderately severe damage, reversible axonal degeneration occurs. If this is so there would be justification for prolonged treatment such as is given in cases of peripheral nerve injury, in which it is known that the period before recovery begins depends upon axonal regeneration occurring in a length of nerve which, if the lesion is situated proximally, will be very considerable.

In poliomyelitis, as after nerve injury, a change in electrical excitability from that of denervated to that of innervated muscle would strongly suggest that axonal regeneration was occurring. Very few serial observations of electrical excitability of muscle in poliomyelitis have been made, but such as are available indicate that once denervation has occurred it is permanent (Moldaver, 1944; Mackenzie, unpublished work). Furthermore, the really worth-while recovery after poliomyelitis occurs within six to eight months after the onset of the disease, and most of it within the first four months (Harry, 1938). If this recovery were dependent upon axonal regeneration it is obvious that the more distal muscles, at any rate, could not have been re-innervated in so short a time, if regeneration has to take place from the cord all the way out to the periphery, at the rate of one to two millimetres a day. It is conceivable that degeneration might occur only in the terminal reaches of the axons of affected neurones, so that the distance to be covered during regeneration would be comparatively short. However, here again electrical evidence of denervation should be present, and so far it is altogether lacking.

It is possible that paralysis may sometimes be due not to damage to the anterior horn cells but to neurones intermediate between the pyramidal and lower motor neurone systems (Schwartz, Bouman and Smith, 1944), in which, if the lesion were at all serious, restoration of function would depend upon the establishment of new routes of communication within the spinal cord; recovery would depend to a considerable extent upon purposeful re-education, and might be a slow affair.

Changes in muscle.—Unless there is a myositis in poliomyelitis the only change that takes place in muscle is the atrophy consequent on denervation. It must be emphasized that the process is an atrophy and not a degeneration (Bowden and Gutmann, 1944). The affected muscles do not require the careful protection such as might be needed if they were the seat of some profound pathological disturbance. Indeed, if there is no hope of axonal

regeneration there is no point in paying special attention to denervated muscles; those in which recovery occurs have retained their neuronal connexions and, apart from being out of action temporarily, are, so far as we know, in no way abnormal. Thus, apart from avoiding overstretching, which is harmful even to a normal muscle, no special mechanical treatment is required, and it is to be hoped that the rigid immobilization which has been a feature of the treatment of poliomyelitis in many centres will soon become obsolete. Miss Kenny condemns splinting outright; this is probably going a little too far since, as will be shown later, splints have a place in preventing overstretching and the assumption of faulty posture. But it must clearly be recognized that splinting should be minimal, and often it is not required at all.

It has been shown that stimulation of denervated muscle with currents of long duration (galvanism) is of considerable value in preventing atrophy (Jackson, 1945), and it should be used routinely in the treatment of peripheral nerve injuries. However, since there is no proof that regeneration of axons plays any significant part in the process of recovery from poliomyelitis, there is no clear indication for employing electrical stimulation at any stage.

Contractures.—The disabilities caused by poliomyelitis are due to destruction of motor neurones and to the development of contractures. For the first there is as yet no remedy; the second is entirely preventable. Everyone knows that a contracture will develop if healthy muscles are allowed to shorten at the expense of paralysed antagonists. This shortening may be prevented by splinting or, better, by frequent passive movements of appropriate joints, the aim being to maintain the normal length of all muscles. It is not so clearly recognized that shortening can occur in paralysed muscles. Denervated muscle undergoes interstitial fibrosis and, given opportunity, the fibrous tissue will contract in exactly the same way as in a scar resulting from injury or infection; here again, the remedy is frequent passive movement. The third cause of stiffness is œdema. The return lymph flow from a limb is dependent upon muscular activity; if there is extensive paralysis and if, to make matters worse, the affected part is allowed to hang down, œdema will result; before long the whole part becomes the seat of a fine interstitial fibrosis which will limit movement of muscles, tendons and joints. Once again the remedy is passive movements together with the maintenance of the limb in elevation.

Irritative phenomena.—In recent years there has been increasing interest in what might be called the irritative phenomena of poliomyelitis; they are of two kinds, sensory and motor, although it is possible, indeed likely, that they are connected. The sensory disturbances occurring in the early weeks of the disease are of four kinds:—(1) The patient may complain of spontaneous pain in the affected part, sometimes of great severity, but without demonstrable sensory changes; (2) there may be cutaneous hyperæsthesia, although it is comparatively rare and usually of short duration; (3) muscles may be tender, and (4) a muscle may be painful when stretched

although not tender to pressure. The cause of these sensory disturbances is not yet fully understood; one thing only is certain, that the damage produced by the virus extends far beyond the anterior horn cells, the posterior root ganglia being frequently affected. The latter would explain the cutaneous hyperæsthesia (which is comparable with that found in herpes zoster), but it is difficult to understand its connexion with the disturbances that are apparently localized to muscle. It is just possible that the pain is sometimes due to an irritative lesion of the sympathetic system, and cases have been recorded in which striking relief of pain in the lower limb followed anæsthetization of the lumbar ganglia (Collins, Foster and West, 1947).

The irritative motor phenomena are all comprised in the controversial term *spasm*. Spasm of the spinal muscles is a frequent feature during the early days of the disease; there is no reason to suppose that it differs from the spinal rigidity that occurs in meningitis, and it regresses as the inflammatory process in the cord subsides. What is much more puzzling is the spasm that sometimes occurs in limb muscles; it is not known whether it is a cause or an effect of pain. It appears to be much less common in this country than in the United States, and in two large epidemics in the Colonies it was found in only very few cases, although a deliberate search for it was not made until the later weeks of the epidemic period. The most satisfactory clinical definition of spasm is painful shortening of a muscle occurring in spite of determined efforts to prevent shortening. It is found in muscles the nerve supply of which has not been completely destroyed, although it may be present at a time when voluntary contractility is absent. Under anæsthesia a full range of movement is possible. It has been shown electro-myographically that the neurones of the affected muscles are in a state of irritability, and there is also a disorder of reciprocal innervation (Watkins, Brazier and Schwab, 1943; Schwartz, *et al.*, 1944). The practical point is that the spasm is due to the primary lesion in the central nervous system, and that it is not harmful except in so far as it tends to the development of contractures, since movements are painful and therefore limited. The spasm gradually dies away along with other disturbances caused by the initial damage to the nervous system.

TREATMENT DURING THE PHASE OF RECOVERY

It must at once be confessed that there has been no recent advance in the treatment of the effects of paralytic poliomyelitis; all the same it is important to know when, and for how long, to apply the few methods of relief that we have at our disposal.

As soon as the illness of onset is over, and provided that the patient is not in great pain, a systematic examination should be made of all the muscles of the head, neck, trunk and limbs. The preliminary examination required for establishment of the diagnosis, often of necessity cursory, is insufficient as a guide to treatment. Usually the paralysis will be maximal within a week of the onset, and a survey made at this time gives a reliable picture of the extent of the damage. In many orthopædic centres muscle charts are now used, and most surgeons are familiar with the system of recording recommended by the Peripheral Nerve Injuries Committee of the Medical Research Council:—

- 5—Contraction against powerful resistance
- 4—Contraction against gravity and some resistance
- 3—Contraction against gravity only
- 2—Movement only with gravity eliminated
- 1—Flicker of contraction
- 0—Complete paralysis

Provided that the patient is handled gently this complete examination is not harmful, although it may be wise not to complete it at one sitting. In children too small to cooperate much patience is needed, but it is surprising how much information may be gained from such manœuvres as tickling the sole of the foot or getting the child to reach for a toy. Once the extent of the paralysis is known the treatment can be planned with precision.

Prevention of faulty posture and overstretching of affected muscles.—The aim should be, not immobilization, but simply the prevention of postures that might lead to contracture, and of abnormal tension on paralysed muscles (Seddon, 1947).

(a) *Spinal and abdominal muscles.*—Unless the patient is an unruly little child a firm mattress is all that is necessary. A lively infant will need a plaster bed or a gas-pipe frame covered with canvas, and some sort of retentive harness may also be required.

(b) *Shoulder.*—The shoulder is largely dependent upon muscles for its stability, and there is therefore much to be said for maintaining it in abduction if the abductors are paralysed, either with a pillow or, in the case of an unruly child, with a plaster or metal abduction splint. Contracture of the adductor muscles can develop very rapidly, which is another reason for maintaining the limb in abduction; 60° is sufficient, and neutral as to rotation.

(c) *Elbow.*—There are those who regard relaxation of a paralysed biceps as unnecessary, the patient being nursed with the affected arm lying alongside the body. Yet in this position the biceps is maintained at what is very nearly its greatest length, and it is therefore preferable to keep the joint in a position of 60° to 90° flexion when paralysis of the flexors is present.

(d) *Wrist.*—The long extensors of the wrist and digits are the only muscles that run any risk of being overstretched by improper posture, and a simple cock-up splint, which must not extend beyond the transverse palmar crease, will give all the support that is required.

(e) *Thumb.*—The metacarpo-phalangeal joint of the thumb, like the shoulder, is largely dependent for its stability upon the short muscles that control it. A small plaster of Paris splint, like a shoehorn, with its broad end lying over the lateral surface of the lower end of the radius and its narrow end curved round into the web between the thumb and index finger, will prevent overstretching of the paralysed thenar muscles.

(f) *Intrinsic muscles of the hand.*—From experience in the treatment of ulnar nerve injuries I am convinced of the need for preventing overstretching of the intrinsic muscles, and there is no very obvious reason why they should not also be protected in cases of poliomyelitis when the long flexors are strong and therefore capable of producing a main-en-griffe contracture. All splints for the intrinsic muscles of the fingers are based on the "lumbricales cuff" first described by Kendall and Kendall (1939). A bar of plaster of Paris or metal crosses the palm at the level of the transverse crease and is joined to two transverse dorsal bars which lie parallel across the metacarpals and the proximal phalanges, the knuckles being exposed between them; the metacarpo-phalangeal joints are held in a position of about 45° flexion.

(g) *Hip.*—The hip should be maintained in the neutral position as in standing, although in small children it may be found more convenient to abduct both joints about 15° in order to simplify nursing.

(h) *Knee.*—The chief danger here is stretching of the posterior capsule of the joint, and the knee should therefore be maintained in a few degrees of flexion.

(i) *Foot.*—The neutral position is correct.

In adults and older children there is no difficulty in maintaining the lower limbs in a correct position by means of small pads under the knees or a sausage-like pad under the mattress, and by supporting the feet at right angles with a board. The patient must not be allowed to slip up the bed.

although not tender to pressure. The cause of these sensory disturbances is not yet fully understood; one thing only is certain, that the damage produced by the virus extends far beyond the anterior horn cells, the posterior root ganglia being frequently affected. The latter would explain the cutaneous hyperæsthesia (which is comparable with that found in herpes zoster), but it is difficult to understand its connexion with the disturbances that are apparently localized to muscle. It is just possible that the pain is sometimes due to an irritative lesion of the sympathetic system, and cases have been recorded in which striking relief of pain in the lower limb followed anæsthetization of the lumbar ganglia (Collins, Foster and West, 1947).

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more, important. This apart, it is difficult to see the value of massage.

Muscle re-education.—Very considerable recovery often occurs spontaneously, but there is no doubt that in the more severe cases much good can be achieved by re-education of muscles. The physiotherapist will have three aims, the relative importance of each varying considerably from case to case:—

(1) Re-education of individual muscles: Certain muscles are of such importance that even when only a little power is present the patient's attention must be concentrated on developing it; there are many obvious examples—the quadriceps, gluteus maximus, and the calf muscle.

(2) The patient should be encouraged to practice movements of parts, such as opening and closing the hand, and the much more complex movement of walking.

(3) Finally, it may be desirable to encourage the development of trick movements when it is apparent that recovery of muscle power is reaching a standstill; for example, the common flexor and extensor muscle masses may become quite effective flexors of the elbow when the biceps and brachialis are completely paralysed.

Under-water exercises are exceedingly valuable, especially in the treatment of the muscles of the trunk and lower limb. It is often astounding how well a seriously paralysed patient can walk in water, and such exercises greatly simplify the transition to walking on land between bars. Exercises with slings and springs have the merit that they can be frequently repeated throughout the day, and a well-trained patient can often do much useful work without constant supervision.

Occupational therapy is essential, not merely for its diversionary value but also as a means of developing coordinated movements.

THE DURATION OF TREATMENT

A serious difficulty is to know when to begin and when to stop a course of treatment which is always time-consuming, tedious and expensive. We do not yet know how long it is before the pathological process in the cerebro-spinal axis subsides, but the excess of protein in the cerebrospinal fluid that we have sometimes found as late as six or eight weeks after the onset of the disease suggests that it is necessary to “make haste slowly” in starting exercises that will call for activity in the anterior horn cells. The best indicator is the appearance of signs of spontaneous recovery; this must show that the inflammatory changes are subsiding, and one need then have no hesitation in starting gentle exercises. The duration of treatment must depend entirely upon the progress revealed by serial muscle charts. Any muscle or segment of the body that remains completely paralysed after four months must be written off as a loss. Occasionally, feeble power returns in such muscles towards the end of the first year or even a little later, but is hardly such as to warrant the retention of the patient in hospital and the intensive efforts of a physiotherapist. Established reaction of degeneration is a most unfavourable sign, and such observations as we have been able to make during the recent epidemic suggest that electrical examination is a reliable guide to prognosis.

A cradle should be used so that the bedclothes do not rest on the limbs. Infants require splints—they are uncontrollable otherwise—and it may even be necessary to splint both lower limbs in a case in which the hip muscles are involved on one side alone. Splints made of plaster of Paris are not very satisfactory since they disintegrate rapidly when wetted with urine. By far the best material is duralumin, and full details for the manufacture of simple splints are available in a paper by Seddon, Hawes and Raffray (1946). These splints were made on a mass-production scale during the epidemics in Malta and Mauritius, and there should be no difficulty in obtaining them in a community where supplies are much less exiguous. The affected limb should not be bandaged tightly to the splint; a simple figure-of-eight at the ankle and one or two turns of bandage above the knee usually suffice. If the child has a powerful calf muscle and paralysed foot extensors the violent pushing-off movements against the foot-piece may be prevented by applying a small plaster "spat" moulded over the dorsum of the foot and ankle in the neutral position, and held in place by the figure-of-eight bandage.

Passive movements.—As soon as the patient is afebrile and free from severe pain the paralysed parts should be put through a full range of movement every day, if possible twice a day. Only in this way can contractures be prevented. Difficulty arises in the case in which muscles are either tender or painful when stretched, yet it is in these cases that full mobility is especially desirable. Deformities are due less to muscle imbalance than to development of contractures, and the painful muscle is very prone to become shortened. These are the cases in which spasm is often present. If one waits until all pain has subsided before attempting to put the limb through a full range of movement organic shortening may by then have developed. Fortunately, gentle passive movement up to and just beyond the point when pain is elicited will as a rule be found effective; the range of movement will often increase rapidly, and I have seen striking cases in which extremely painful limbs became painless and mobile after frequent passive movements carried out over a period of a few weeks. It is in these cases that Miss Kenny and her disciples particularly favour the application of hot packs.

Heat.—The value of heat for the relief of pain in poliomyelitis has been recognized for over a generation. For the early pains of the disease immersion in a warm bath is most valuable. Hot packs or dry heat are often soothing, but, as many American workers and we ourselves have found, packing according to the Kenny technique by no means always relieves the painful shortening of muscle that we now call spasm. However, it is worth trying. Spasm may persist for several months, it may seem to resist all treatment; but I have not yet seen a case in which muscle shortening was permanent, provided that there was no relaxation in the effort to attain full mobility by passive, and later active, movement.

Massage is of use in getting rid of œdema in an extensively paralysed limb, but elevation of the part and frequent passive movement are equally, if not

INJURIES OF THE KNEE

By ROLAND BARNES, M.B., F.R.C.S.

Lecturer in Orthopædic Surgery, Glasgow University; Orthopædic Surgeon, Western Infirmary, Glasgow.

THE knee is a complicated joint, and is ill-adapted to withstand rotational strains, which are of frequent occurrence in both sport and industry. The knee joint is entirely dependent for its stability upon the collateral and cruciate ligaments, and the muscles which surround the joint. Of these structures by far the most important is the quadriceps muscle, for it is the first line of defence against strain. Quadriceps insufficiency is often responsible for persistent weakness of the knee following injuries or operations on the joint.

Wasting of the quadriceps is almost inevitable following an injury of the knee joint, and it is of fundamental importance to prevent wasting, so far as possible, by active exercise. The simplest and safest exercise is that of bracing the knee, but the contractions must be both vigorous and sustained, and repeated at frequent intervals throughout the day.

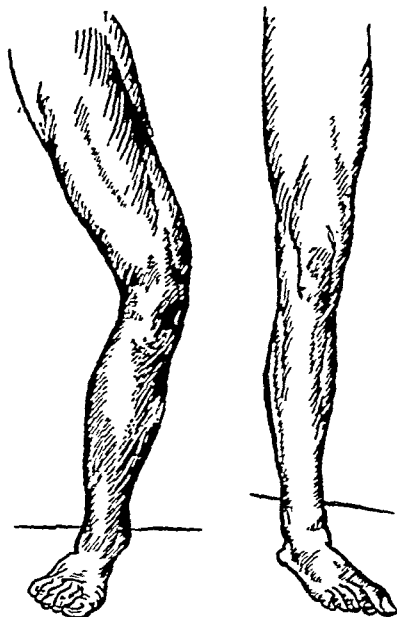


FIG. 1.—Mechanism of a tear of the internal semilunar cartilage. The knee must be flexed and the tibia abducted and externally rotated on the femur while weight is borne on the limb.

FIG. 2.—Mechanism of a tear of the external semilunar cartilage. The knee must be flexed and the tibia adducted and internally rotated on the femur while weight is borne on the limb.

INJURIES OF SEMILUNAR CARTILAGES

A torn cartilage is always caused initially by a weight-bearing rotational strain of the flexed knee, and is a common injury in footballers and miners. External rotation and abduction of the tibia on the femur result in the internal cartilage sliding towards the centre of the knee joint, and if weight is being borne on the leg at the same time the cartilage will be split by the grinding action of the tibia on the femur (fig. 1). This is a common injury and accounts for tears of the internal cartilage being five or six times as frequent as those of the

external cartilage, which are caused by a weight-bearing internal rotation adduction strain of the tibia on the femur (fig. 2).

FOR HOW LONG SHOULD RECUMBENCY BE MAINTAINED?

When the lower limbs and spinal muscles have been seriously involved it has been customary to keep the patient recumbent for long periods—twelve to eighteen months—even when muscle charts show no substantial improvement after, say, six months. This has been done in the belief that such small late increases in power as may occur are worth waiting for. Recently, Ransahoff of New York has taken the bold step of getting his patients up early; he claims that the attempted resumption of normal posture is of far greater value to the patient than the feeble little improvements that may occur during the later months of prolonged recumbency. Like Miss Kenny he even goes so far as to withhold supportive apparatus in cases in which, according to generally accepted ideas, external mechanical aid is required. He works on the assumption that in a well-treated limb, however weak, the ligaments of unsupported joints will not stretch. I had the privilege of seeing many of his cases and, although I was compelled to disagree with some of his ideas, I was greatly impressed with the agility and excellent gait of patients who had fairly extensive paralysis. The impression was gained that they had been got on to their feet before they had forgotten how the lower limbs were intended to be used.

During the past epidemic we proceeded with much hesitation and caution along the same lines, allowing patients to get up two to four months after the onset of the disease. After a patient had been got up, first in water, then between bars, and finally with sticks, important muscles, such as the abductors of the hip, the erectores spinæ and the abdominals, some of them seriously affected, were examined regularly for signs of deterioration. They appeared in only one case, and in that patient progress became satisfactory when the pace was slightly reduced. At this stage it is impossible to say which practice is right, the old one or the new, but it seems likely that in the past we have erred on the side of excessive caution, perhaps even to the detriment of limbs which, if more activity had been allowed, would have suffered less from the effects of general atrophy.

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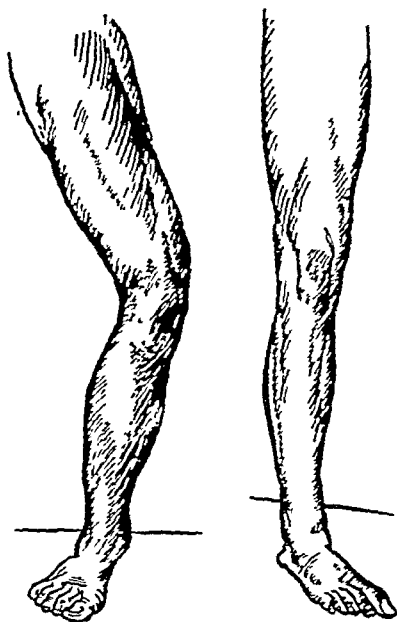


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external cartilage, which are caused by a weight-bearing internal rotation adduction strain of the tibia on the femur (fig. 2).

Clinical features of tear of a semilunar cartilage.—The classical symptoms and signs of a torn cartilage are:—

- (1) Pain and tenderness over the damaged cartilage.
- (2) Locking of the knee in a semi-flexed position followed within a few hours by swelling of the joint.
- (3) Sudden unlocking, either spontaneously or following a manipulation of the knee, with immediate relief of pain and discomfort.
- (4) Recurrent attacks of locking, pain, and effusion, of less severity than after the initial injury, and often following a trivial twist or strain of the knee.

If the above clinical picture is accompanied by a normal skiagraphic appearance of the joint, a tear of the cartilage can be diagnosed with confidence. There are, however, many tears of the cartilage which are not accompanied by these classical symptoms. A history of locking is often regarded as essential in the diagnosis of a torn cartilage, but true locking only occurs when the tear involves the anterior half of the cartilage, resulting in a mechanical block to full extension (fig. 3). Tears which are confined to the posterior horn of the cartilage are never accompanied by locking. Locking of the knee is not always due to a torn cartilage; a loose body or a fracture of the tibial spine may cause a mechanical block to extension. Painful conditions of the front of the knee, such as bruising of the retropatellar fat pad, or a strain of the coronary ligament of the semilunar cartilage, will result in a reflex inhibition of extension of the joint which closely simulates true locking. In these conditions (with the exception of a loose body) extension of the knee is gradually restored over a period of days or weeks, and there is no sudden unlocking as in a torn meniscus.

Diagnosis of tear of the internal cartilage.—There is a history of a weight-bearing abduction external rotation strain of the tibia on the femur while the knee is flexed (fig. 1), followed by immediate and severe pain over the inner side of the joint. If the lesion is of the bucket-handle type the diagnosis is easily made, as the classical symptoms and signs of a torn cartilage are present, accompanied by tenderness over the anterior end or middle part of the cartilage (fig. 5).

In a tear of the posterior horn of the internal cartilage the symptoms and

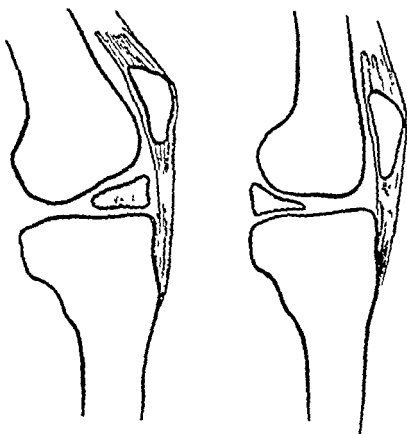


FIG. 3.—A mechanical block to full extension of the knee, or "locking", can only occur when the tear involves the anterior part of the cartilage.

signs are more equivocal. There is no true locking; the patient merely complains of a momentary loss of control and has difficulty in localizing the pain. There may be tenderness over the posterior horn of the internal cartilage (fig. 5), but it is often absent and synovitis is seldom severe. McMurray's test is of the greatest value in the diagnosis of these lesions of the cartilage. It is performed as follows:—

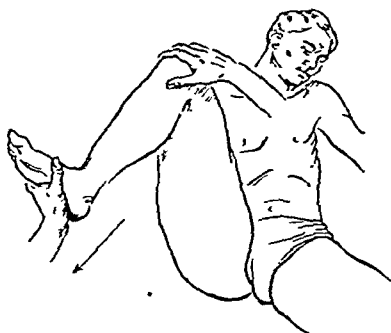


FIG. 4.—McMurray's test for a tear of the posterior horn of the internal cartilage. The knee is flexed to its fullest extent and the foot is externally rotated and the leg abducted at the knee. Holding the leg and foot at this angle the knee is slowly extended.

"The patient must be recumbent and relaxed; the surgeon standing on the side of the injured limb grips the foot firmly, while the knee is bent to its fullest possible range, until the heel approaches or touches the buttock. The foot is now rotated externally, and the leg abducted at the knee. Holding the leg and foot at this angle, the knee is slowly extended (fig. 4). With the alteration of the angle of the joint any loose portion of the internal cartilage is caught between the articular surface of the femur and the tibia, and the sliding of the femur over the abnormal portion of the cartilage is accompanied by an appreciable click and pain, which the patient states is the same as he has already experienced when the knee gave way. If no click can be produced by these movements properly conducted it may be safely considered that the internal cartilage is normal posteriorly" (McMurray, 1943).

Occasionally in children or adults with lax knees a click may be obtained in a normal cartilage; it differs, however, from the click of a tear of the posterior horn of the cartilage in that it is *not* accompanied by pain or discomfort.

Diagnosis of tear of external cartilage.—Tears of the external cartilage are caused by a weight-bearing adduction internal rotation strain of the flexed knee (fig. 2). In a bucket-handle tear of the external cartilage the classical symptoms of pain over the outer side of the joint, sudden locking and unlocking of the knee may be present, but in the majority of cases there is merely a feeling of weakness or slipping in the outer side of the joint, followed by tenderness over the anterior or posterior horn of the cartilage. Tears of the anterior part of the cartilage often cause a peculiar snap, which is heard towards the end of *active* extension of the joint, and at the same time the whole joint appears to shiver. This snap is also a characteristic feature of a congenital discoid cartilage, in which the embryonic disc-shaped meniscus persists into adult life. McMurray's test is usually positive in lesions of the posterior horn; the test is performed as described for lesions of the internal cartilage, except that the tibia is internally rotated and adducted as the knee is gradually extended from a position of full flexion.

Radiography.—X-ray examination of the joint should never be omitted

even when the classical symptoms and signs of a cartilage lesion are present. Radiography will demonstrate a loose body, if it contains bone, and any irregularity of the articular surface, or a fracture of the tibial spine.

DIFFERENTIAL DIAGNOSIS OF CARTILAGE LESIONS

The following lesions of the knee joint may produce symptoms resembling those of a tear of one of the semilunar cartilages:—

Loose body.—A loose body may cause symptoms very similar to those of a cartilage lesion. There is often momentary locking and acute pain when the body is trapped between the articular surfaces. The pain, however, is usually referred to different parts of the joint each time the knee locks, and occasionally the loose body may be palpable. Loose bodies which are giving rise to symptoms can usually be demonstrated radiologically.

Strain of the internal lateral ligament.—An abduction strain of the extended knee may cause a partial tear or a complete rupture of the internal lateral ligament. There is usually tenderness over the upper attachment of the ligament to the inner femoral condyle (fig. 5), and if the tenderness is over the ligament at the level of the joint it may indicate a combined ligament and cartilage injury (fig. 5). There is often an effusion into the joint, and *limitation of extension by muscle spasm* which simulates locking. It differs from the locking of a cartilage lesion in that there is no sudden unlocking, and the joint gradually straightens as the pain and muscle spasm subside. A complete rupture of the ligament is accompanied by abnormal lateral mobility of the joint.

Rotational strains of the knee.—A severe *non-weight* bearing rotational sprain of the knee may strain the attachment of a semilunar cartilage to the anterior aspect of the upper end of the tibia. Acute pain is felt over the front of the joint, and the patient may complain of a sensation of "locking". There is gross limitation of both flexion and extension by muscle spasm, and tenderness over the front of the knee by the side of the patellar ligament. The symptoms gradually subside with the firm application of a crêpe bandage and quadriceps exercises, but it may be several days or weeks before full extension of the knee is restored.

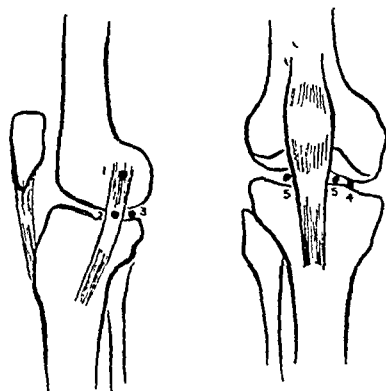


FIG. 5.—Points of tenderness round the knee joint: (1) Strain or rupture of internal lateral ligament; (2) sprain of deep fibres of internal lateral ligament which may be combined with tear of internal semilunar cartilage; (3) damage to posterior horn of internal cartilage; (4) damage to internal cartilage usually bucket-handle or anterior horn tear; (5) lesions of retropatellar fat pad.

Enlarged retropatellar fat pad.—Enlargement of the fat pad is usually associated with osteoarthritic changes in the knee, and seldom causes symptoms in patients under forty years of age. Nipping of the fat pad causes pain in the front of the joint, and tenderness on each side of the patellar ligament (fig. 5). There may be pseudo-locking, but there is no sudden unlocking as in cartilage lesions. X-ray examination may reveal osteoarthritic changes in the joint.

Fracture of the tibial spine.—This injury occurs in adolescents and is usually caused by a blow on the flexed knee, which drives the femur backwards on the tibia. There is a tense effusion of blood into the joint, and the displaced fragment of bone causes a block to full extension of the knee, which resembles the locking of a displaced cartilage. The diagnosis can usually be made on the history of the injury, the rapidity and tenseness of the effusion, and the severe muscle spasm which results in marked limitation of all knee movement in addition to the block to extension. The clinical diagnosis is readily confirmed radiologically.

TREATMENT OF A TORN SEMILUNAR CARTILAGE

The majority of tears of the cartilage are in the central portion, and show no tendency to heal. If a patient sustains a tear of this portion of the cartilage,

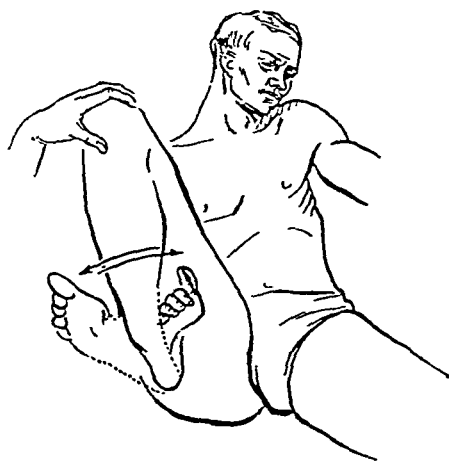


FIG. 6.—Manipulation of a "locked" knee joint. The knee is fully flexed and the tibia rotated from side to side. In tears of the internal cartilage the tibia is then rotated inwards to the full extent and the knee suddenly extended. In tears of the external cartilage the tibia is externally rotated as the knee is extended.

recurrent displacements are inevitable with rotational strains of the knee. The peripheral attachment of the cartilage is well supplied with blood vessels, and tears and detachments in this area can heal if the knee joint is splinted at the time of the initial injury. It is impossible to determine by clinical examination whether a tear is in the substance of the cartilage or its peripheral attachment. Conservative treatment is advised after the initial injury, in the hope that the tear is in the peripheral attachment.

Conservative treatment.—If the knee is locked the joint should be manipulated as soon as circumstances permit. Unless the patient is seen immediately after the accident, the manipulation is best

performed under anæsthesia. The knee is fully flexed and the tibia rotated from side to side (fig. 6). In tears of the internal cartilage the tibia is then

rotated inwards to the full extent and the knee suddenly extended. If the lesion is of the external cartilage, the tibia is externally rotated as the knee is extended. A successful manipulation is indicated by restoration of full extension, often accompanied by a pronounced click, and the patient will state that the knee is comfortable. If the manipulation is unsuccessful, operative treatment should be advised.

Following the manipulation a firm compression bandage and a back splint are applied, with a small pad behind the knee to keep the joint slightly flexed. Quadriceps exercises must be practised assiduously to prevent wasting of the thigh muscles, as the future stability of the joint greatly depends upon the restoration of full muscle power. If there is persistent swelling and tenderness in the joint the splint is retained for three to four weeks or longer. A full range of movement is rapidly regained by active movements of the knee after the splint has been removed. Any residual wasting of the quadriceps muscle is treated by exercises against gradually increasing resistance, cycling being particularly helpful.

A recurrent displacement of the cartilage cannot be cured by manipulation, and removal of the torn cartilage is indicated. The "cures" of the unqualified practitioner are obtained in knees in which adhesions have formed following strains of the joint, or in an early osteoarthritis of the knee.

Operative treatment.—If a cartilage has been displaced on more than one occasion it should be removed without further delay, for osteoarthritic changes are likely to occur following repeated derangements of the joint. If the diagnosis is in doubt conservative treatment is indicated. An exploratory arthrotomy is an unjustifiable procedure, for even a wide exposure of the anterior part of the knee joint may fail to reveal a tear of the posterior horn of the cartilage. The unsatisfactory results of cartilage surgery can be attributed to inaccurate diagnosis, failure to remove the whole of the damaged cartilage, neglect of the postoperative treatment and, the greatest tragedy of all, infection of the joint.

It cannot be over-emphasized that removal of the cartilage is but an incident in the programme of treatment. At the end of the operation a firm compression bandage is applied to prevent effusion into the joint. A persistent effusion is a common cause of disability; it results in stretching of the ligaments and capsule of the joint, and leaves a lax and unstable knee.

Quadriceps exercises are of the greatest importance and are begun on the day after operation and continued until the normal bulk and power of the thigh muscles are restored. Active movements of the knee are begun after the tenth day, but weight bearing is not permitted for at least another week. Too early weight bearing causes recurrent effusion and retards recovery. The knee joint should not be subjected to rotational strains until the thigh muscles are sufficiently developed to protect the knee from injury. In favourable cases athletic games can be begun six to eight weeks after operation.

CYSTS OF SEMILUNAR CARTILAGES

Cystic degeneration of the cartilages is not common. The cyst is usually situated in the middle third of the cartilage, the external cartilage being involved in the majority of cases.

The patient complains of aching pain over the affected cartilage, which is aggravated by exercise. The cyst is usually no larger than a walnut, is situated accurately over the joint line, and is more prominent when the joint is fully extended. The swelling is very tense and may be mistaken for an exostosis. Cysts invariably recur after local removal or aspiration, and the only satisfactory treatment is to remove the whole of the cyst and the affected cartilage.

LESIONS OF THE INTERNAL LATERAL LIGAMENT

The clinical diagnosis of a sprain or rupture of the internal lateral ligament has been described when discussing the differential diagnosis of tears of the internal cartilage. A simple strain of the ligament is treated by the application of a firm crêpe bandage to prevent effusion, and a back splint is applied to the knee for ten days, with the joint slightly flexed. Weight bearing is then permitted, and the inner border of the heel and sole of the shoe is raised a quarter of an inch to protect the inner side of the knee from abduction strains. The raise on the shoe is retained until all pain and tenderness have subsided. Quadriceps exercises should be practised assiduously throughout the treatment.

Complete rupture of the internal lateral ligament is a serious injury, and if it is not treated efficiently the patient is left with a very unstable knee joint. A plaster cast is applied from the groin to the ankle, with the knee in almost full extension and the tibia *adducted* on the femur. The plaster is retained for at least two months, and quadriceps exercises are performed to prevent wasting of the thigh muscles.

LESIONS OF THE EXTERNAL LATERAL LIGAMENT

The external lateral ligament is sprained or ruptured by a forcible adduction strain of the tibia on the femur when the knee is in full extension. This type of violence is unusual in the knee joint, and consequently lesions of the external lateral ligament are much rarer than those of the internal lateral ligament. The tear or rupture usually occurs at the lower attachment of the ligament to the head of the fibula. Treatment is similar to that for lesions of the internal ligament, except that the joint is immobilized with the tibia *abducted* on the femur.

RUPTURE OF ANTERIOR CRUCIATE LIGAMENT

The ligament is attached to the front of the tibial spine, and passes upwards, backwards, and outwards to the intercondylar surface of the external

femoral condyle. The ligament may be ruptured by a forcible abduction or hyperextension strain of the knee, and the injury is frequently associated with a tear or rupture of the internal lateral ligament.

The patient complains of severe pain in the knee, and there is a rapid effusion of blood into the joint. Tenderness is diffuse, and all movements of the joint are limited by muscle spasm. An adequate examination cannot be made without anaesthesia. A rupture of the anterior cruciate ligament is demonstrated by abnormal forward mobility of the tibia on the femur when the knee is slightly flexed (fig. 7). The stability of the internal lateral ligament should always be tested at the same time.

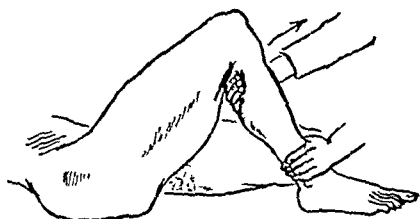


FIG. 7.—Method of testing for rupture of the anterior cruciate ligament.

Treatment.—A plaster cast is applied from groin to toes, with the knee slightly flexed, and the head of the tibia pushed *backwards* on the femur. The joint is immobilized for a minimum of twelve weeks, and intensive quadriceps exercises are practised after the first three days. The results of conservative treatment are good, provided the diagnosis is made promptly and the treatment is efficient.

An untreated rupture of the anterior cruciate ligament leaves the patient with instability of the knee, which is greatly aggravated if the thigh muscles are weak and wasted. With each step the tibia tends to glide forward on the femur, and the disability is especially severe when descending stairs. In these cases every effort must be made to restore the normal bulk and power of the thigh muscles. Reconstruction of the torn ligaments is seldom satisfactory, and if the disability persists after intensive quadriceps exercises the stability of the joint may be improved by the use of a knee cage.

RUPTURE OF THE POSTERIOR CRUCIATE LIGAMENT

This is an uncommon injury. It is usually caused by the tibia being driven backwards on the femur when the knee is in right-angled flexion. The injury is demonstrated by the abnormal backward mobility of the tibia on the femur. Treatment is similar to that of a ruptured anterior cruciate ligament, except that the tibia is pulled *forwards* on the femur while the plaster cast is applied.

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DISLOCATIONS OF THE ELBOW

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DISLOCATIONS of the elbow joint are frequently accompanied by fracture. Thus whenever a dislocation is suspected it is necessary to establish whether or not a fracture is also present. This can only be done with certainty by means of radiological examination. The interpretation of skiagrams of the elbow is not easy, especially in children, and an understanding of the development and growth of the bones forming the elbow joint is necessary, as dislocations occur most often in children.

THE EPIPHYSES

The lower end of the humerus has four special centres, three of which are fused to form the lower epiphysis, whilst the fourth, for the internal condyle, is separated from these by an extension downwards of the shaft. This

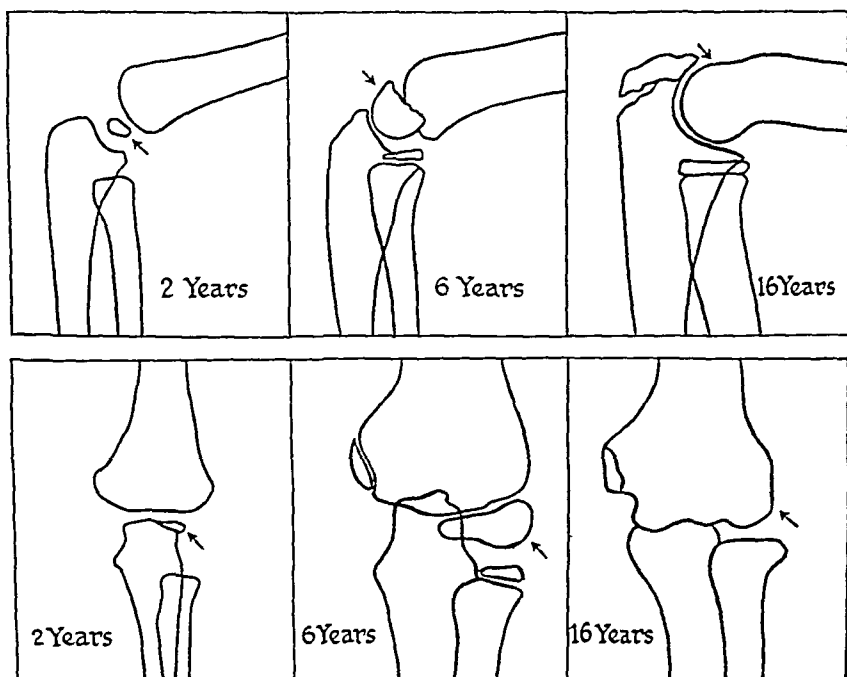


FIG. 1.—Diagram showing ossification of the epiphyses of the elbow. Arrow points to the capitulum.

extension forms the bone between the internal condyle and the trochlea (the

part in relation with the ulnar nerve behind); so that the lower margin of the humerus may be said to be made from five centres, of which four are epiphyseal.

The centre for the capitulum comes first, in the second to third year, followed by that for the inner condyle in the fifth to eighth year; the trochlear centre appears at about the age of eleven, and the external condylar nucleus a year later. Thus these centres for the lower end of the humerus are all present a few years before puberty. After puberty the extension of the ossification of the shaft takes place, and the three centres of the lower epiphyses fuse with each other and with the shaft at about the age of seventeen, followed by junction of the inner condyle with the shaft within a year. The upper end of the radius begins to ossify about the sixth year and the upper end of the ulna during the tenth year. Both unite between the ages of seventeen and twenty.

Any of these epiphyses, such as the capitulum or medial epicondyle, may become separated at the time of the dislocation during the growth period when they are vulnerable, and may be overlooked following the reduction of a dislocation, if their exact significance is not appreciated.

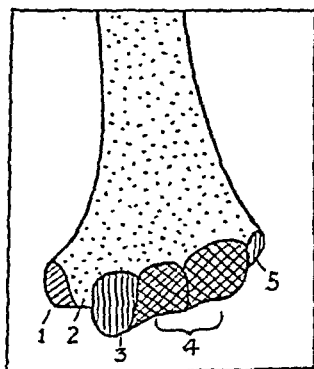


FIG. 2.—Diagram showing the five different ossifications which are concerned in forming the lower end of the humerus. The dotted area is shaft which reaches the end at 2; 1, 3, 4 and 5 are centres of inner condyle, trochlea, capitulum and outer condyle, respectively. Note that the capitular centre is also responsible for the outer part of the trochlea. (*Anatomy of the Human Skeleton—Frazer.*)

TYPES OF DISLOCATION

The term *dislocation of the elbow* is usually meant to infer dislocation of both bones at the elbow. Dislocations may take place in a posterior direction or in a postero-medial or postero-lateral direction. Anterior displacement with fracture of the olecranon is known to be very rare. The mechanism of the injury is usually a fall on the outstretched hand, although it may be the result of direct violence.

Dislocation of the upper end of the radius may take place by itself but it is an uncommon accident. The mechanism of this injury is discussed briefly later.

DIAGNOSIS

An exact diagnosis must first be established; although this may be arrived at by careful clinical examination, skiagrams should always be taken for confirmation.

A supracondylar fracture of the elbow is the most likely injury to confuse with a posterior dislocation. Although these injuries are easy to distinguish

radiologically they are not always so clinically. In posterior dislocation the normal relationship of the olecranon to the epicondyles is absent; also there

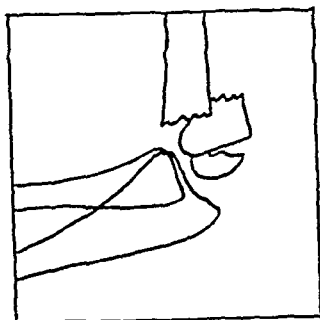


FIG. 3.—Supracondylar fracture of the elbow with backward displacement.

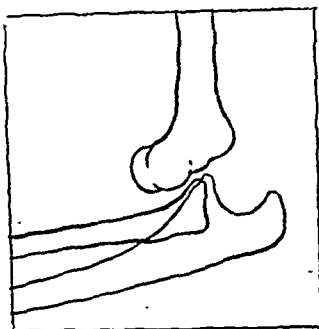


FIG. 4.—Posterior dislocation of the elbow.

is a relative fixity and immobility of the elbow joint in dislocation compared with the increased mobility which is present in a supracondylar fracture.

The age-group of the patient may also help, for whereas in the first decade supracondylar fracture is the more common accident, in the second decade dislocation is more often encountered. A supracondylar fracture is rarely, if ever, found in the adult.

TREATMENT

Dislocation of the elbow, whether complicated by fracture or not, requires immediate reduction. Reduction becomes increasingly difficult with the passage of time, and the longer it is delayed the greater the danger of damaging the joint structures. When complete muscular relaxation by anaesthesia is obtained the reduction can generally be carried out without the use of force.

When the ulna lies in a postero-medial or postero-lateral relation to the humerus it should first be pressed into a directly posterior relationship.

The upper arm is fixed by an assistant, and gentle traction is applied to the forearm in the axis in which it lies, that is, in flexion. It is unnecessary to apply strong traction or to extend the joint. It is quite unnecessary, and may be harmful, to hyperextend the elbow in order to unlock the coronoid process from the olecranon fossa.

When the operator has to work single-handed without assistance the method of four-direction traction may be employed. By this method a dislocation of the elbow joint is easily reduced by one operator with a minimum of injury to the joint. Figure 5 shows the method.

With the patient lying on his back a folded sheet is placed round the chest and secured on the opposite side of the table from the operator. This fixes the chest and gives countertraction. A 4-inch muslin bandage, long enough to reach to the floor, is then placed round the arm above the elbow. This bandage is tied so that it forms a loop, the lower end of which is about six inches above the floor. The foot is

placed in this loop for traction downwards. A similar bandage is placed round the forearm with the elbow flexed at 90° and is tied behind the operator; this gives traction laterally. The patient's wrist is grasped with the operator's left hand, thus producing traction upwards, and the operator's right hand is free to manipulate the elbow joint.

The patient is anæsthetized and, when muscle relaxation is complete, the operator applies traction in four directions: (1) by leaning backwards; (2) by pressing downwards with the foot through the loop in the bandage; (3) by pulling upwards with the left hand, and (4) with countertraction across the chest.

When reduction is obtained a collar-and-cuff sling is applied with the elbow flexed, the hand being fixed in the sling a few inches below the chin level. Flexion should not be acute and the radial pulse should be felt at the wrist before leaving the patient.

As a rule a posterior plaster splint is not necessary to maintain reduction but may be added if re-dislocation is feared. A post-reduction skiagram should always be taken.

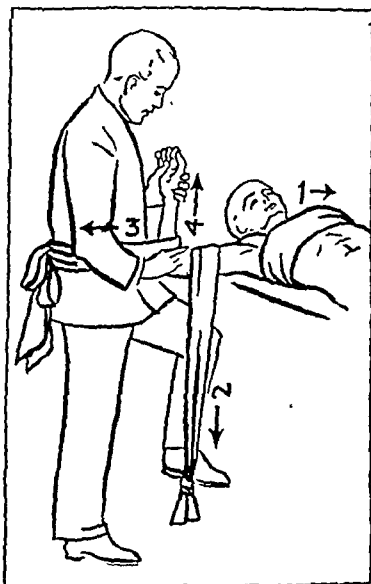


FIG 5.—Dislocation of the elbow reduced by traction in four directions.

POSTOPERATIVE CARE

Shoulder, wrist and finger movements may be instituted in twenty-four hours. In uncomplicated dislocations the elbow should be immobilized for two to three weeks. If there is a complicating fracture it may be necessary to prolong the period of fixation by a further two weeks. When movement is allowed, function of the elbow should be restored by the patient's unaided activity. Massage and passive movements of the joint should be avoided.

COMPLICATIONS

The following complications sometimes accompany dislocations of the elbow:—

- (1) Fracture accompanying dislocation
- (2) Nerve injuries
- (3) Traumatic ossification at the elbow
- (4) Failure of reduction

Complicating fractures are rare with dislocations in the first decade, when the ends of the bones are largely cartilaginous. In the second decade they are common, due chiefly to the vulnerability of the epiphysis of the medial epicondyle at this period. In the third decade, again fractures are rare, but after that, and especially in elderly people, they may occur.

The medial epicondyle is most commonly fractured (in association with postero-lateral dislocation of the elbow), being pulled away by the attachment of the strong internal lateral ligament. Most of such fractures are in

reality epiphyseal separations. Other fractures found complicating dislocation of the elbow are fractures of the coronoid process, the head of the radius, the external epicondyle of the humerus, and the capitulum.

Injury to the ulnar nerve usually occurs when dislocation is accompanied by fracture of the medial epicondyle. The injury is caused by contusion or stretching, and spontaneous recovery is the rule. More rarely a rough spicule of bone in the region of the medial epicondyle may cause irritation to the ulnar nerve, when it may be necessary to remove the spicule or transplant the nerve to the front of the elbow. Injury to the radial nerve may occur, but is rare.

Traumatic ossification at the elbow is due to trauma, either the result of the accident or caused by excessive zeal in treatment. When dislocation occurs, muscle and capsule insertions into the periosteum are avulsed and a subperiosteal hæmatoma forms. Thus with avulsion of the brachialis anticus from the ulna, or avulsion of the forearm muscles from the condyles, hæmorrhage occurs in these regions in front of the joint, and ossification may take place in these hæmorrhagic areas. This is all the more likely to happen if the elbow is roughly handled either at the time of reduction or in the early post-reduction period. Passive stretching and forcible movements before the periosteum is firmly reattached to the bone should be avoided.

Failure of reduction is a complication that should not arise if post-reduction skiagrams are a routine.

DISLOCATION OF THE UPPER END OF THE RADIUS

In rare cases the head of the radius may be dislocated anteriorly. The radial head is retained in its articulating position with the lesser sigmoid cavity of the ulna by the orbicular ligament and so long as the ulna remains intact the interosseous membrane also constitutes a strong support. Thus anterior dislocation of the head of the radius is almost invariably accompanied by a fracture of the shaft of the ulna. Operative repair of the ruptured orbicular ligament may be necessary. It is in this type of dislocation that injury to the radial nerve may occur.

SUMMARY

The treatment of elbow dislocations should entail:—

- (1) Radiological examination before reduction and preliminary investigation to exclude nerve injuries.
- (2) Reduction with full relaxation under general anæsthesia with the elbow in flexion without resort to excessive force.
- (3) The taking of post-reduction skiagrams.
- (4) Immobilization by cuff-and-collar splint for two to three weeks to allow completion of the process of healing within the joint.
- (5) The avoidance of any forced movements, manipulations or massage in the postoperative period which may tend to the formation of new bone (myositis ossificans) around the joint.

TUBERCULOSIS OF BONES AND JOINTS

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THE problem presented by tuberculosis of bones and joints is mainly one not of surgery, but of sociology. The infecting organism is known to be either the bovine or the human type of tubercle bacillus, which gains access to the body either in milk from tuberculous cows, through the lungs, or by direct implantation. Direct implantation may occur in those who have to deal with tuberculous meat or material.

It should be recognized and generally accepted that no milk should be supplied to the community from a cow that is tuberculous. But no one who visits the sheds in which many cows spend a large part of at least the winter months can doubt the fact that they are favourable to the spread of tuberculosis among cows, and as a consequence among human beings. Assistance given to the farmers to enable them to improve the conditions under which their cows are housed should be a great economy, not only in the prevention of unnecessary suffering, but also even in the saving of human life.

It should also be accepted that the housing conditions of the people and the means of segregation should be such as to prevent the risk of spreading infection to the other members if a case of pulmonary tuberculosis occurs in a family. The development of colonies for the tuberculous, where a man or woman who had been infected could live in pleasant surroundings doing useful work with the minimum of risk to others, would assist also in reducing the incidence of tuberculosis of bones and joints. There is little doubt that if the problem were tackled at its sources, within a reasonable period it would cease to exist.

Although tuberculosis of bones and joints may be caused by either type of tubercle bacillus it is agreed that in children the more common has been the bovine type introduced into the body by tuberculous milk; the percentage has been reduced recently by the more general and efficient pasteurization of milk. In adults, although some cases may be caused by the bovine bacillus, a high proportion are due to the human type. Apart, however, from its prevention, the question of whether the infection in any one patient is of human or bovine origin is academic—it does not affect either the treatment or the diagnosis.

METHOD OF SPREAD

It is probable that the bacillus after introduction into the system infects lymph glands and, when their resistance is overcome, travels by the blood stream to bones and joints. If this is so, it can readily be understood that a

local diminution in resistance caused by an injury and a resulting contusion may in certain patients favour the development of the typical tuberculous lesion. This is much more likely to occur if the general condition of the patient is poor.

Sites.—Tuberculosis of bones or joints may be primarily diaphyseal, metaphyseal, epiphyseal or synovial, but in time may spread in any direction in the bone or joint. The infection occurs more commonly in the lower limb and the spine than in the upper limb. This may be because the lower limb and spine are more liable to injury.

Whatever the site of the primary lesion may be, during the course of treatment some other lesion may develop. This may be a silent one affecting some other bone or joint, which on the slightest suspicion should be carefully investigated. It may be pulmonary or renal tuberculosis, although this is not common, and very occasionally it may be tuberculous meningitis.

DIAGNOSIS

In general this depends upon the history and upon the clinical signs.

History.—Whilst it is known that tuberculosis is not hereditary, home conditions may predispose to infection. There are many instances in which several members of a family have been infected. This fact, to which too much significance should not be attached, may, if tuberculosis of a bone or joint is suspected, lead to an earlier provisional diagnosis than would otherwise be possible. This is of great importance, for early treatment is vitally necessary and should be instituted without waiting until the diagnosis is definite. This necessitates a careful explanation of the position to the patient and his relatives to prevent unnecessary anxiety. The symptoms usually come on gradually and they may be associated with an injury. The first sign noticed may be slight pain, with some swelling of a bone or joint.

Clinical signs and symptoms: General.—The oft-repeated statement that tuberculosis of a bone or joint is a local manifestation of a general disease must be constantly remembered. In the early stages of a tuberculous infection of a bone or joint the patient usually looks ill. The signs indicating the presence of a tuberculous lesion are:—

- (1) The appearance of ill-health.
- (2) Localized pain at times—particularly when the hip is affected—associated with night cries.
- (3) Swelling of the joint, with muscle spasm preventing movement and causing deformity.
- (4) Atrophy of the muscles controlling the joint.
- (5) Slight rise of temperature.
- (6) Abscess formation.
- (7) Bone destruction shown by radiological examination. This may not be present in the early stages. If the infection is of the synovial type, rarefaction of the bones only will be seen.

Some of these signs may not at first be evident, nor are some ever present if the shaft of the bone only is affected.

Clinical tests.—The diagnosis is complete if tubercle bacilli can be found in the pus from an abscess, or if a guinea-pig inoculated with the pus develops tuberculosis. A negative test does not preclude the possibility of tuberculosis. Other clinical tests that can also be made are the Mantoux intradermal test and the patch test. They are of value, particularly if negative. The sedimentation rate, if raised, is a sign of infection, and therefore a useful aid in diagnosis.

Tests involving an operation.—A biopsy, in which a portion of synovial membrane is excised from a joint and examined microscopically and bacteriologically, with the opportunity that this gives to examine the inside of the joint, is of value. This is particularly so in cases which while undergoing treatment do not take the normal course, and in which the diagnosis cannot otherwise be confirmed. When the lower limb is affected an inguinal lymphatic gland is sometimes excised for examination. If found to be tuberculous this is corroborative evidence of tuberculosis of one of the joints of the limb.

TREATMENT

As tuberculosis is basically a general condition in which there is local evidence of disease, the treatment must be general and local, and it must be primarily conservative. The late Sir Henry Gauvain, defining conservative treatment, used these words: "By conservative treatment is meant the adoption of all measures which tend to improve the patient's general health, increase his powers of resistance to tuberculous disease, and preserve or restore the part or parts attacked, in contradistinction to radical treatment, which aims at the cure of the disease by the removal of the local lesion". From this it follows that conservative treatment does not mean merely non-operative treatment, for any treatment, whether surgical or otherwise, used with the object of eradicating or overcoming the effects of disease, is in this sense conservative.

General treatment.—In this is included treatment and care of both the body and mind of the patient. So far as possible a life in the open air is essential. The patient should be in a hospital, removed from the smoke and fog of the town, on a well-drained site where the maximum sun can be obtained. Regular exposure of the body to the sun and air to improve the general well-being is necessary but must be done gradually and with caution. For the beginning of sunlight treatment the early morning sun is best, but even to it the body should be exposed only by degrees. Good food, well served, is essential. Protein hydrolysate is sometimes of value in improving general nutrition. Congenial occupation is necessary. There should be facilities for occupational therapy which can be carried out during recumbency and a good hospital library is needed. Ciné films are useful in relieving the tedium of enforced immobilization. Lectures on subjects of general interest are valuable.

In the general treatment of the patient the hospital almoner plays an important part. She it is who discusses any economic or domestic difficulties which are troubling him, in this way possibly relieving his mind from anxieties. The almoner's work may prevent the premature cessation of treatment, which sometimes occurs when patients are worried about their home conditions and feel they must return home to deal with them. It is essentially the object of general treatment to relieve anxiety, to improve well-being and so enable the patient to gain a philosophical outlook. In this the cooperation of the patient's general practitioner is of the greatest value, particularly if he is able to pay periodical visits to the hospital.

Treatment by drugs.—Recently, experiments have been made with three substances, sulphetrone, streptomycin and para-aminosalicylic acid, all of which have definite antituberculous properties. Streptomycin has certain toxic effects, and streptomycin-resistant strains of tubercle bacilli are apt to develop. Sulphetrone and streptomycin have been used in combination with some success. Para-aminosalicylic acid has no known toxic effects. Insufficient work has as yet been done to assess the results of the use of these drugs, but as they are the first so far found to have any effect on tuberculosis, their discovery is of great significance.

Surgical treatment in general.—Abscesses when large should be aspirated through a valvular opening which seals itself when the aspirating needle is withdrawn. It is essential in doing this to use the most scrupulous aseptic precautions; failure in this may cause secondary infection with serious consequences. The pus so obtained should be used for diagnostic purposes. If a definite diagnosis has been made, aspiration is required only when an abscess is large, shows signs of pointing, or is in some way embarrassing the patient. In extra-articular lesions removal of the extra-articular focus of infection has sometimes been advocated with the object of preventing the spread of disease. This, however, is seldom advisable and, if tried, often ineffective. When a local infection has occurred as a result of a direct implantation, particularly in the finger, amputation of the affected part is necessary.

The essential surgical treatment is immobilization involving external fixation of the limb or joint, with traction if the hip or knee is involved, until the condition has become quiescent, with the addition in certain cases of internal fixation. The aim of treatment is not to obtain a movable joint but to arrest the disease. The ultimate function of the joint depends upon the degree of destruction which has occurred before it becomes quiescent. When can the condition be considered quiescent? This is decided on the following points:—

- (1) The absence of muscular spasm and pain.
- (2) Steady diminution of swelling and the disappearance or calcification of abscesses.
- (3) The X-ray appearance showing consolidation of the affected area.

(4) The return of the sedimentation rate to normal.

(5) An increase in weight and general improvement in health.

Whereas, when major joints are infected, patients should in theory continue treatment by immobilization until quiescence has occurred, in adults, because of its general effect, the length of treatment has sometimes to be cut down. It is a question of deciding in each individual case what is best to be done for the patient regarding him as a whole.

TUBERCULOSIS OF THE SPINE

Physical signs.—Apart from the general symptoms, the diagnosis is made chiefly on the basis of localized pain and rigidity of the spine. This is often accompanied by a feeling of weakness on the part of the patient, who when sitting in the upright position supports his spine by using his arms (similar signs may occur in subacute osteomyelitis of the spine). An abscess is often present and the X-ray shows destruction of bone. In sacro-iliac disease the signs are often indefinite, and the first sign indicating the presence of tuberculosis may be an abscess.

Treatment.—For the treatment of this condition many methods have been evolved. They range from plaster of Paris beds to frames of various types, the object of all being immobilization of the spine. Plaster of Paris beds are of special value when there is considerable deformity of the spine, but Jones's straight frame is a most satisfactory splint for the routine treatment of the average case. It requires, however, special skill on the part of the nursing staff if it is to be really effective.

Robert Jones's frame. This consists of a metal framework, made to fit each patient, on which a saddle consisting of an outer covering of basil leather stuffed tightly with lambs' wool is placed. On this a patient can lie with his spine relatively immobilized in comparative comfort. The side bars of the frame, both for the body and the legs, are malleable and, when moulded to the body, limit lateral movement. The frame extends from the lower cervical region to below the knees and is used for lesions of the spine from the mid-dorsal area to the sacro-iliac joints.

When the lesion occurs at a higher level than the mid-dorsal region additions have to be made to the frame. In the upper dorsal region a head-piece on which the head rests is added, and if the cervical spine itself is involved, a sunken head-piece into which the head fits is used.

Although the frame should prevent a deformity from occurring, the question may be asked, "What should be done to correct a deformity which already exists?" The answer to this is that no attempt should be made to open up or separate vertebral bodies which as a result of a disease have come together, but the deformity can be masked rather than corrected by hyper-extending the spine above and below the diseased area, and so improving the general balance of the body.

Paraplegia.—This is a complication of tuberculosis of the spine which is relatively uncommon. It may be caused by œdema occurring around the spinal cord, abscess formation compressing the cord, or by pressure of bone.

As a rule in milder cases paraplegic symptoms disappear with immobilization. Occasionally, however, operative treatment is necessary. This takes the form of either costo-transversectomy or laminectomy, depending upon the presumed cause of the paraplegia. If it is thought that the paraplegia is due to pressure by an abscess, costo-transversectomy is done. In this operation the posterior part of a rib at the required level is excised together with the adjacent transverse process, and access is so obtained to the front of the vertebræ affected, and the abscess evacuated. If on the other hand the paraplegia is due to pressure of bone, then a laminectomy is performed, the removed laminæ being replaced by bone grafts to support the weakened vertebræ.

Splintage after immobilization.—When the period of immobilization is completed—a minimum of twelve months for adults and rarely less than



FIG. 1.—Posterior spinal support with collar for tuberculosis of the upper dorsal region of the spine.

two years for children—the frame is replaced by a spinal support—the Jones's posterior spinal support (fig. 1). If the upper dorsal area is affected, a collar is added and strapped to the support, and if the cervical spine is affected, a doll's collar is used also. For lesions of the fifth lumbar vertebra and the sacro-iliac joint a short spica is at first used instead of a posterior spinal support, being later replaced by a sacro-iliac support.

The spinal support should be worn until firm consolidation has taken place or for a minimum period of two to three years. In children it is best to maintain the support until the end of the growing period, unless sound bony fusion has taken place.

Internal fixation.—In adults, when the condition has become quiescent, in addition to the external fixation provided by the support, internal fixation of the vertebral laminæ by spine grafts is of great value, particularly if

there is any lateral displacement of vertebræ or if bony fusion of vertebral bodies has not taken place. The object of the grafts is to fix the laminæ of the affected vertebræ together with two above and two below this area, and so minimize the risk of a sudden strain or jarring awakening a quiescent lesion into activity, which might happen if there were only a fibrous ankylosis. It is important that the spine should have reached a quiescent stage before grafting is done, otherwise the graft may tend to hold vertebral bodies apart and so prevent that fusion which is so important in the healing process. The type of graft often used is the twin tibial graft. Instead of this a shaped tibial graft or iliac bone may be used. In children a grafting operation

should be done only for special reasons, such as a lateral deformity.

Spine grafting: twin tibial grafts.
—Two strips of bone are cut from the shaft of the tibia and placed on the laminae after these have been exposed and made raw. The grafts should extend to two vertebrae above and two below the affected area. It is usual for the patient to be immobilized on the frame for about three months after the grafting operation, the subsequent course being similar to that already described. Operative fusion of the sacro-iliac joint is rarely necessary.

THE HIP

Physical signs.—The hip is usually flexed and adducted, movement is painful, and the early symptoms may be referred to the knee. Two conditions are sometimes confused with tuberculosis of the hip. Local symptoms may be simulated by a strain of the hip joint, but the general signs already mentioned are not then present. In osteochondritis of the hip (Perthes's disease) there is a limp with restricted movements, but the symptoms are much milder in degree than in tuberculosis.

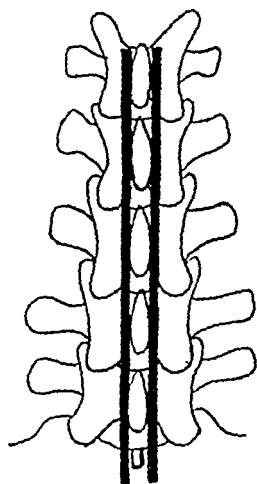


FIG. 2.—Fusion of the spine. Twin tibial grafts in position on the laminae.

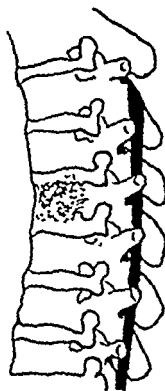


FIG. 3.—Lateral view of spine showing tibial graft in position on laminae.

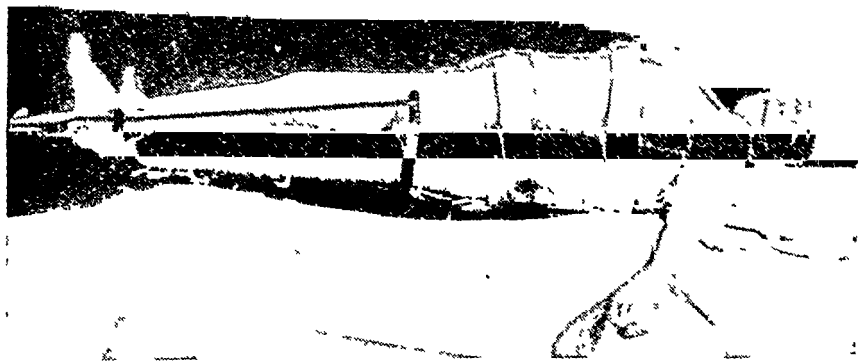


FIG. 4.—Patient on Jones's abduction frame for tuberculosis of the hip.

Treatment.—As in the treatment of the spine, different types of splint have been devised for this condition but as a routine method a Jones's abduction frame, if used carefully, is an effective and satisfactory splint. It differs from the straight frame for the spine in that the leg pieces are

prolonged beyond the end of the feet so that extension can be applied to the legs, and the splint is so made that the affected leg can be abducted to any degree required.

If severe adduction and flexion deformity of the hip are present, some have advocated manipulative correction before placing on the splint. It is found, however, that in most cases continuous and steady traction, particularly if in the early stages the limb is supported on a pillow placed on the splint, will gradually correct the deformity. If the deformity cannot be corrected it is better to wait until the quiescent stage has been reached and then to correct it by operation.

Operative treatment.—This may take the form of transtrochanteric or subtrochanteric osteotomy to correct a deformity, or of one of the various types of fusion operation. In some patients in whom, in spite of traction, the hip gradually subluxates because of continuous erosion of the acetabulum, operative treatment is needed. It is also of value in cases in which fibrous, and not bony, ankylosis has occurred, for in these cases there is a strong tendency to recurrence of the deformity. It is best then to adopt an operative procedure which is extra-articular, so avoiding opening up the affected area of bone. In children two methods in particular have been found effective:—

(1) *Ilio-femoral fusion.*—In the Wilson operation—useful for children—a flap of bone is turned down from the outer table of the ilium and hinged on its lower extremity, it is bent over and embedded in a cleft cut in the great trochanter (fig. 5).

This method results in the formation of a bony bridge extending from the ilium to the femur and, if successful, stabilizes the hip joint. In adults the flap of bone from the ilium is replaced by a tibial graft.

This operation is not advisable when there is continuous erosion, either of the acetabulum or of the head of the femur, until complete quiescence has occurred—which may be a very prolonged period.

Ischio-femoral fusion (Brittain's operation).

—The operation consists of dividing the shaft of the femur—

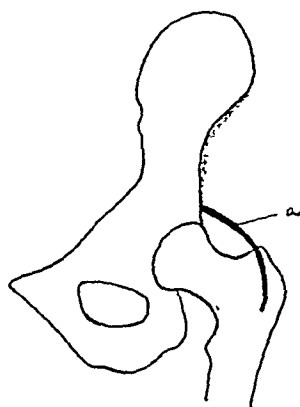


FIG. 5.—Ilio-femoral fusion. (a) Flap of bone turned down from ilium and embedded in great trochanter.

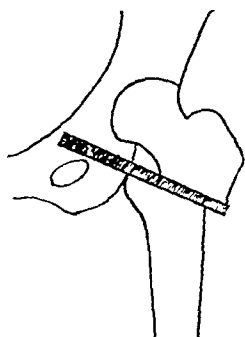


FIG. 6.—Ischio-femoral fusion showing tibial graft joining shaft of the femur to the ischium (Brittain's method).

a transtrochanteric osteotomy—making a cleft in the ischium and passing a graft cut from the tibia between the ends of the divided femur into this cleft, then displacing the lower fragment of the shaft of the femur inwards (fig. 6). The object of the operation is to form a permanent bony bridge uniting the femur to the ischium.

After both these operations a long plaster spica has to be used to immobilize the joint until fusion is complete.

COMPLICATIONS OF RECUMBENCY

As the treatment of tuberculosis of the spine and hip involves recumbency this in itself may cause certain complications:—

Renal calculus.—An uncommon complication which can be avoided by regular tilting of the patient to ensure adequate drainage for the kidneys and by insisting that the patient has adequate fluids to make up for the dehydration which may result from long exposure to the sun. The calculus of calcium phosphate usually disappears on the resumption of the upright position. The possibility of a calculus should be suspected if after turning the patient into the prone position—which is done periodically to inspect the back—hæmaturia occurs.

Pressure sores.—These occur surprisingly seldom and can be entirely prevented if special nursing care is taken. In particular it is necessary to provide careful padding and protection for a prominent bony kyphosis.

THE KNEE

Physical signs.—No special physical signs are presented by the knee and other joints of the limbs. If, as is often the case, the infection of the knee is of the synovial type there may be no early radiological signs.

Treatment is carried out on a Thomas's bed splint. The knee is supported by slings and held in position by strapping extensions applied below the joint. Great care has to be taken that subluxation of the tibia does not occur. This is prevented by a pad applied to support the upper end of that bone. In children, when quiescence has been attained, a guarding plaster is applied to the knee, from the upper part of the leg to a few inches above the ankle and this is worn with a caliper splint (fig. 7). In adults, unless the infection has remained synovial and a useful range of movement has been retained



FIG. 7.—Caliper and guarding plaster applied for tuberculosis of the knee. Straps holding the leg in position in caliper are not shown.

the safest procedure is by operative excision, to arthrodesis the joint, the patient when ready to get up, doing so, as in the case of children, with a guarding plaster and caliper. The use of this is continued until fusion has taken place. Opinions have varied as to whether it is better to have a knee stiff in the straight or slightly flexed position. This should depend upon the individual need of the patient with a preference for the straight position in the average case. Occasionally amputation of the limb has to be considered.

OTHER BONES AND JOINTS

The remaining bones and joints of the limbs are treated in plaster of Paris in the optimum functional position.

The ankle: foot.—Plaster of Paris should hold the ankle at right angles. Walking after the quiescent stage has been reached should be begun in plaster. Astragalectomy is sometimes needed. In severe cases amputation may be necessary in adults.

The shoulder.—This is treated in plaster of Paris in the right angle abducted position, which position may be attained by gradual corrective plasters. When quiescent the joint should be fused. Probably the best method of doing this is by excising the joint, turning the acromion into a cleft in the humerus, and reinforcing this by a tibial bone graft. The aim should be to fix the shoulder in about 70° of abduction with 20° of flexion, with a few degrees of external rotation.

The elbow.—The elbow is held flexed at about 90° —either more or less—depending upon the work of the patient, until quiescent.

The wrist.—The position of ankylosis is 20° of dorsiflexion. When quiescent, unless firm bony ankylosis has occurred, a fusion operation, using a tibial bone graft extending from the lower end of the radius to the posterior surface of the carpus, is needed.

The carpus and fingers.—These should be fixed in plaster in the slightly flexed position.

CONCLUSION

The best method of dealing with tuberculosis of bones and joints is by prevention: each patient is evidence of failure on the part of the community to face the problem. Nevertheless, the great majority of patients, if given adequate treatment in suitable conditions, can hope that the result will be satisfactory and will enable them to become independent and self-supporting citizens.

AMPUTATIONS

By JOHN CHARNLEY, M.B., B.Sc., F.R.C.S.

*Lecturer in Orthopædics, Manchester University; Assistant Honorary
Orthopædic Surgeon, Manchester Royal Infirmary.*

MANY points of interest in amputations tend to be purely technical, and therefore lie more in the province of the surgeon, but for the general practitioner there are certain aspects on which he would do well occasionally to refresh his mind; these are:—(1) The principles which govern the design of the ideal stump; (2) the principles underlying the technique of emergency amputation; (3) the domiciliary supervision of the recent stump.

THE DESIGN OF THE IDEAL STUMP

The upper extremity.—In the *arm* and *forearm* the form of the stump and the level of section offer no special problem; usually the level is self-evident and the preservation of maximum length is of paramount importance. The level of amputations in the *fingers*, however, sometimes gives rise to difficulty as a result of an old dictum that one should never amputate through the proximal interphalangeal joint but always through the metacarpo-phalangeal joint, because the proximal phalanx has only the tendons of the lumbrical and interossei to flex it. My own experience is against this; I have seen many fingers so amputated which have had powerful flexion, and which to the heavy manual worker seemed to be of some value and certainly did not impair the function of the hand by "getting in the way". If the patient is of any class other than the heavy labourer then the amputation should always be through the shaft of the metacarpal itself. In the case of the index finger a careful amputation through the shaft of the metacarpal gives a most gratifying result, and it almost seems to compensate the patient for loss of the digit instead of leaving the bulbous knuckle as a perpetual reminder of his misfortune.

The lower extremity.—Because of the special function of weight bearing the lower limb is the true subject of stump design. In England the experiences of the Ministry of Pensions have resulted in only two stumps being recognized as "ideal"; these are, the below-knee amputation containing 4 to 5 inches of tibia measured from the joint line, and the above-knee amputation containing from 9 to 12 inches of femur measured from the great trochanter (the larger length being for tall subjects). As regards technique it is recommended that the bone-end is covered only with skin and deep fascia; that no attempt be made to include muscle in the flaps; that the nerves are sectioned at the level of the muscle and that they are not drawn down, crushed, injected with alcohol, or tied with ligatures. This treatment of the nerves is thought to render less likely the start of nerve pain in amputation stumps. As it is now recognized that an amputation neuroma is a physiological response to division of a nerve, it is obviously

better to allow the neuroma to form at the end of the stump where it will be free from pressure in a modern prosthesis.

The ideal lengths of the above-knee and below-knee stumps have been evolved as a compromise between (1) the longest length of stump which is likely to be free from circulatory complications, and (2) the mechanical requirements of the limb-fitter.

In estimating the maximum length of stump likely to be free from circulatory complications, it is only necessary to imagine an amputation through the lower third of the tibia to realize that the last 4 inches of such a stump would consist of nothing more than skin-covered bone, and this at a site which is notorious for its tendency to varicose ulceration, even in the normal patient. In the same way amputation at the level of the femoral condyles leaves thin skin tightly stretched over a bulbous bone-end, and there is no muscle above it for nearly six inches. This is one of the reasons why the limb-fitting surgeon has condemned the "end-bearing stump". The records of the Ministry of Pensions from the 1918 war have shown that the majority of Syme amputations have eventually fallen to re-amputation at a higher level after a variable period of years.

As regards the limb-maker's mechanical requirement, it must be remembered that the end-bearing stump, i.e., through the knee or at the ankle, cannot be accommodated in an elegant prosthesis because, in the case of the thigh, the knee mechanism has to be outside the bulbous-ended stump, and in the case of the ankle it is impossible to design a Syme's prosthesis which a female could wear without its being very noticeable.

In Canada and America common practice is in agreement with the above opinions with the exception that more attempts to use end-bearing stumps are still countenanced. It has been suggested, and with a strong possibility that this may be true, that the Canadian winters, being dry, cause less circulatory disturbance than the winters we are accustomed to in England. For this reason the Syme amputation is held in good favour by the Canadians and Americans.

Unorthodox amputations.—The principles just outlined are those which underly the present teaching in the amputation of election; but it must not be forgotten that there are many unorthodox amputations still functioning, or which have functioned well for many years. Personally, I would always try a Syme amputation on a young man rather than an immediate below-knee amputation, although suitable cases for a Syme amputation are rare. Again, I would never be frightened of attempting an amputation through the forefoot (Lisfranc), as I have seen several patients who were able to walk well in an ordinary shoe after filling the toe with cork, with the added advantage of being able to walk short distances barefoot. Between the Syme and Lisfranc, however, nothing should be attempted; experience has shown that the Chopart (mid-tarsal) amputation is not a good amputation as the lack of tibialis anterior causes the heel to be drawn up and the weight to fall on the forward-tilted scar.

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- (1) Primary closure: Careful closure in layers with multiple sutures and drainage with tubes.
- (2) Delayed closure: One or two sutures; closure later.
- (3) Delayed closure: No sutures, skin traction to flaps, Thomas's splint; closure later.
- (4) Delayed closure: Closure with three or four sutures over pack of vaseline gauze or of dry gauze; closure later

With adequate chemotherapy, and provided that the patient has not to be moved for a long journey shortly after the amputation, all these methods will yield a high percentage of clean wounds, but the method which I wish to advocate here is that of closure over a dry pack, because of my personal experience with the method (Jack and Charnley, 1943) and because I believe that it can be better justified by reason than most others.

Delayed closure with the use of a dry gauze pack.—In all emergency amputations the wound should be regarded as more or less heavily inoculated with bacteria. The proliferation of the inoculum is favoured by blood clot as the organisms are unreached by the antibacterial defences of the body. Merely to suture a wound loosely or to insert tubes does not prevent the accumulation of clot—indeed the interior of a tube is an ideal site; a tube merely allows the infected and liquefied clot to escape. In the same way a vaseline gauze pack encourages oozing, as it delays clotting, as do the paraffined walls of the Kimpton tube, and it only allows overflow to the exterior. A dry gauze pack on the other hand does not encourage oozing, and when the pack comes to be removed there will usually be no black clot visible, except possibly on the bone-end itself. If the ends of the pack are allowed to project from the corners of the wound so as to make contact with the external dressings, capillarity will allow tissue fluid to escape. It is futile to use a "dry" pack if this is totally enclosed in the wound; it is essential that the ends project at each side. A second important action of the pack is in securing hæmostasis by providing a firm base for the external bandage. The skin flaps are thus under gentle pressure between the external dressings outside and the internal pack inside; the difficulty of applying a firm compression dressing to a loose stump without a pack is considerable. Finally, a third action of the pack is to prevent the skin flaps from shrinking—it is in fact a form of skin traction applied internally.

The success of this method depends largely upon the care with which the second stage of the operation is performed, and success can only result if the surgeon completely understands the rationale of the method. The pack must be removed under aseptic precautions *not later than the fifth postoperative day*. The reason for this is that if left any longer the ingrowth of granulation tissue will result in fresh bleeding when the pack is removed and a new clot will accumulate. When the pack is removed it must therefore be done with the utmost gentleness so as not to invite bleeding. Finally, the wound must be dressed with a carefully applied pressure dressing to prevent the accumulation of serum.

CARE OF THE STUMP

In the home the practitioner is likely to encounter recent cases of amputation waiting for the fitting of an artificial limb. It is important that he should be able to judge if the patient is being well instructed in the care of the stump, and be able to make suggestions if the patient has not understood his instructions.

THE THEORY OF EMERGENCY AMPUTATION

The country practitioner may be faced with an emergency amputation following road or agricultural injuries which his fellow in the city is unlikely to encounter owing to the proximity of accident centres to industrial areas. In the industrial towns the practitioner may have to sever a crushed limb in order that the patient may be removed to hospital, but this will require nothing more than common sense and a sharp instrument. The experience of two world wars has reaffirmed the importance of two primary objects in emergency amputation:—(1) to aim for the longest possible primary stump and (2) to plan the amputation with flaps for delayed closure.

The long primary stump.—Obviously a long primary stump will make it possible for an ideal stump to be fashioned by a specialist at some later date; but it must not be forgotten also that many unorthodox long stumps have given good service despite current dogma, and without re-amputation; there is no point therefore in encroaching too near the elective site. Emergency amputation is technically easy in the low sites of section of the limb, as these sites are the narrow parts above the ankle and the knee where the amount of muscle to be divided is minimal. In this connexion a word of warning must be uttered against the temptation to disarticulate at a joint as an emergency measure, and even more so against the temptation to disarticulate at the knee, although in theory this might sound very attractive as being free from shock, hæmorrhage or channels of infection. Experience has shown that the expanded ends of these bones are covered only with a thin layer of skin and mild infection drags on for weeks until the elective re-amputation may have to be performed with an unhealed terminal ulcer.

In aiming for a generous length of primary stump the bone should always be divided at a higher level than the skin in order that flaps can be fashioned of sufficient length to cover the bone-end. In other words, a guillotine operation should *never* be performed (sectioning the bone and soft parts at the same level) because healing is slow, the patient is miserable, and elective amputation will generally have to be risked in the presence of an unhealed terminal ulcer.

Points in technique.—Having divided the skin, fat, and deep fascia as near to the primary skin wound as common sense dictates, the circular incision can be converted into rectangular flaps by two lateral incisions. The flaps are raised, preferably with the deep fascia, to the level of bone section as estimated from the thickness of the limb. The muscle should now be sectioned with a circular sweep of an amputation knife at the level of proposed bone section. An amputation knife is preferable to the small "Bard-Parker" type of knife which results in "section by a thousand cuts", which often means that the same vessel may be cut at two levels close to each other. No special treatment of the periosteum is advocated. In severing the tibia it is essential always to remove the sharp anterior angle on the subcutaneous border; omission of this detail may result in an ulcer on what otherwise might have given a permanent stump without further re-amputation.

Delayed closure.—Having removed the damaged limb the surgeon is now faced with the decision of how to cover the bone-end with the skin flaps. The following possibilities present themselves:—

attitude and insist that the pain will soon disappear. To be too sympathetic to a patient who retains a leather finger-stall is doing him a disservice, and the patient should be encouraged to expose the stump to the air and to

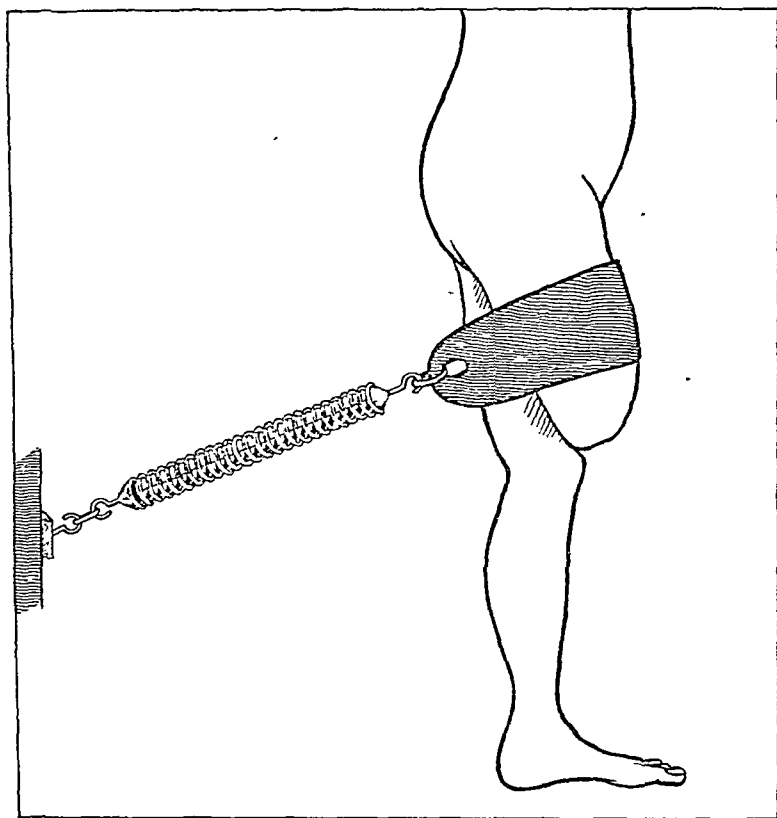


FIG. 2.—Type of stump exerciser which can be used at home.

experiment in getting familiar with any unpleasant sensation in contact with external objects. In my own experience only a few cases of painful amputation stumps in the fingers have yielded satisfactory results from attempts to remove neuromas; those cases which are worth while exploring are those in which the patient does not show other signs of apprehension and the tenderness is localized to a "trigger" point which can be touched off with the pressure of a pencil always in the same spot. Cases in which the patient flinches from pressure applied over a wide area are rarely benefited by excision of the neuromas.

Reference

Jack, E. A., and Charnley, J. (1943): *Brit. med. J.*, ii, 131.

While awaiting the fitting of a stump two objects must be attained:—(1) the shrinkage of the stump into a conical shape, and (2) the prevention of flexion contracture in the joint proximal to the amputation.

The *conical stump* can be achieved by careful bandaging, and this can only be done if the patient, or the relative, has been shown how to re-apply the bandage morning and evening. It is worse than useless to have a bandage which can be slid off like a hat or one that gets its purchase on the stump by circular constricting turns just proximal to the end, which have the effect of causing the end itself to become bulbous. In my experience the most effective bandage is one which looks rather amateur because it is improvised turn by turn and is not a regular "textbook" bandage which is applied to a

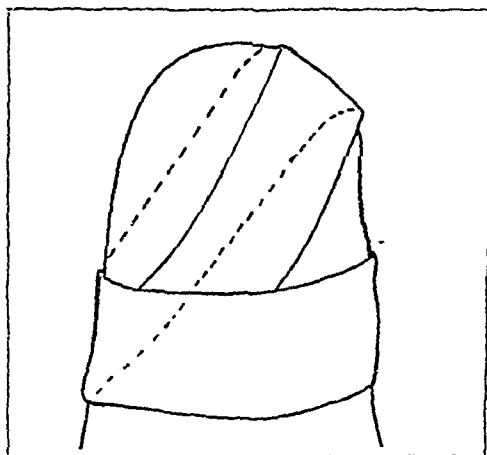


FIG. 1.—Oblique pressure turn and circular retention turn which form the basis of the bandage by continuous repetition.

fixed pattern. The essential thing about the bandage is that it should include numerous oblique turns, each of which covers part of the end of the stump and which is held in place by the intervening circular turns. This arrangement of alternating oblique pressure turns and circular retention turns is indicated in figure 1. As the bandage is arriving towards the end, a few turns should be passed round the body, if it is a thigh amputation, to assist in holding the bandage on. The bandage itself should be of the widest crêpe

obtainable, and for the compression of a thigh stump it is best to stitch two 6-inch bandages end to end.

The *flexion contractures of the joint* proximal to the level of amputation can be prevented by regular exercises to strengthen the muscles. These exercises are also of value in preparing the power of the stump for motivating the prosthesis, and they also have a beneficial influence on the morale and prevent a feeling of apprehension becoming permanent. This feeling of apprehension is the natural result of a recent and disconcerting "phantom" limb. A stump exerciser should be improvised from a sling, and cord attached to a weight and pulley or to a spring exerciser, which can be purchased from any sports-shop (fig. 2).

In *finger amputations* the use of the other digits is of such importance that it is self-evident; but the attitude of the practitioner towards a painful amputation stump after removal of a finger needs to be carefully studied. The vast majority of painful digital stumps are probably hysterical in origin, and the practitioner would do well to adopt a robust and cheerful

operate on men who work at the coal face. In the remaining cases we conducted investigations to eliminate other causes of sciatica, such as spondylolisthesis, osteoarthritis of the hip joint or tuberculous osteitis of a vertebra. Local foci of infection were searched for and corrected but wholesale extraction of teeth was never indulged in. Also, to people whose general health was below par, tonics and artificial sunlight were administered.

We then chose those cases with severe scoliosis, greatly restricted spinal movements, loss of an ankle jerk and objective sensory loss in a specific dermatome. Next, those with few signs but whom we judged to be particularly good types and whom we thought to be suffering from severe pain. Those patients who had had frank attacks of neuritis elsewhere in the body or those who showed signs of rheumatism, such as deformation of the joints, and those who gave a history of toxic synovitis were eliminated, and also those with severe tenderness over the distribution of the sciatic nerve, as we regard severe local tenderness as a sign of toxic interstitial neuritis.

SIGNS AND SYMPTOMS

Of the 200 patients, 173 were males and 27 females. The ages ranged from nineteen to sixty; the greatest number (101) were in the fourth decade of life (50.5 per cent.), and the next largest was 52 in the third decade (26 per cent.). Patients were operated upon both from the Services and from civilian life: 94 (47 per cent.) came from the Services, 106 (53 per cent.) were civilians, and all grades of worker, from the heavy manual worker to the sedentary worker, were represented.

Symptoms.—Only 76 (38 per cent.) of the 200 patients gave a history of a definite injury to the back; in the remaining 124 (64 per cent.) no history of injury was obtained. The average duration of symptoms was thirty-five months; the shortest period of suffering being one month and the longest thirty years. If the extremes are excluded, average duration of pain was about eighteen months to two years.

Approximately one-third (34.5 per cent.) of the cases had begun with gradual onset of sciatic pain—a smaller proportion (26.5 per cent.) with gradual onset of backache. Twenty per cent. had experienced sudden onset of backache as the initial symptom of their illness, whilst 13.5 per cent. had experienced sudden onset of sciatic pain. The remainder had begun with gradual or sudden combined backache and sciatic pain. In the whole series 18 per cent. had enjoyed intervals of complete freedom from pain in the course of the illness, whereas in 164 (82 per cent.) the symptoms had been continuous but of varying severity, that is to say they had never been completely free from pain. In 83 cases (41.5 per cent.) the pain was in the right leg and in 107 (53.5 per cent.) in the left leg. The leg pain was exacerbated by straining, coughing and sneezing in 149 cases (74.5 per cent.).

Physical signs.—In those cases which were ambulant a marked limp was present in 137 (68.5 per cent.). The extremely severe cases were confined to bed and were unable to stand or walk. Flattening of the normal lumbar hollow occurred in 151 cases (75.5 per cent.); this flattening was at times very marked, in some cases amounting to a lumbar kyphosis in the region of the 3rd and 4th lumbar spinous processes. Scoliosis was outstanding in 128 cases (64 per cent.). The direction of the deformity was variable, some cases showing convexity to the affected side, others to the unaffected side,

LOW BACKACHE, SCIATIC PAIN AND THE HERNIATED NUCLEUS PULPOSUS

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FROM January 1941 to December 1944, 500 patients suffering from sciatica were referred to the Neurosurgical Unit at the Newcastle General Hospital for investigation and treatment. Of these 500 cases, 200 were operated upon for a herniated nucleus pulposus, and laminectomy was performed. The object of this communication is to give the criteria by which the patients operated on were selected from the main group; to present in detail the symptoms and signs in the cases in which a herniated nucleus pulposus was found at operation so as to throw light on the problem of diagnosis; to explain the mechanism of the pain in those cases in which no great abnormality was found at operation; to describe our operative findings and to appraise our operative methods; and to review our long-term postoperative results.

The criteria by which 200 cases were selected for operation.—In all there were 200 cases under review:—

Complete immobilization in bed for at least three weeks had failed to give satisfactory relief. Most of the patients had received all kinds of formal physiotherapy, including radiant heat, diathermy, infra-red rays and massage: fourteen had been immobilized completely in plaster of Paris beds for long periods; sixteen had been treated by spinal manipulation under general anaesthesia; about one-third, at some time or other, had had injections of novocain into various muscle groups or into the sciatic nerve itself. In many cases attempts had been made to stretch the sciatic nerve by various ingenious methods.

In the early groups of cases the first sorting was made on psychiatric grounds. Those with frank psychiatric disorders were eliminated by our psychiatrist, Dr. Munro; there were few of these. On our own judgment we eliminated many others—those who appeared to be nervous types or who, we thought, were exaggerating their disability, and those whose general behaviour in the wards was unsatisfactory. For example, many could walk long distances to the cinema but could do little else; also there were the mischief-makers who agitated others to complain. Of course we know this is a very arbitrary method and often unjust in assessing a man. In simple terms, according to our own personal experiences, a patient was selected as the right type or eliminated as the wrong type.

Then, on purely physical grounds, the poor physical types were eliminated; also those with varicose veins, and those already downgraded or ill from complaints other than sciatica. In addition, men were excluded who had to return to particularly heavy jobs, such as a "blacksmith's striker", although later selection on those grounds changed; now we commonly

operate on men who work at the coal face. In the remaining cases we conducted investigations to eliminate other causes of sciatica, such as spondylolisthesis, osteoarthritis of the hip joint or tuberculous osteitis of a vertebra. Local foci of infection were searched for and corrected but wholesale extraction of teeth was never indulged in. Also, to people whose general health was below par, tonics and artificial sunlight were administered.

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SIGNS AND SYMPTOMS

Of the 200 patients, 173 were males and 27 females. The ages ranged from nineteen to sixty; the greatest number (101) were in the fourth decade of life (50.5 per cent.), and the next largest was 52 in the third decade (26 per cent.). Patients were operated upon both from the Services and from civilian life: 94 (47 per cent.) came from the Services, 106 (53 per cent.) were civilians, and all grades of worker, from the heavy manual worker to the sedentary worker, were represented.

Symptoms.—Only 76 (38 per cent.) of the 200 patients gave a history of a definite injury to the back; in the remaining 124 (64 per cent.) no history of injury was obtained. The average duration of symptoms was thirty-five months; the shortest period of suffering being one month and the longest thirty years. If the extremes are excluded, average duration of pain was about eighteen months to two years.

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whilst some showed an alternating type of scoliosis. Some patients, when assuming the erect position after forward flexion of the spine, exhibited a peculiar "unwinding" effect of their scoliosis. We consider this momentary unlocking or unwinding effect an important diagnostic sign. Restriction of spinal movements was most marked on attempted forward flexion of the spine; 54 (27 per cent.) had restriction of spinal extension. Restriction of lateral flexion and rotation of the spine was not an obvious feature. Severe paravertebral tenderness was found in only 19 cases (9.5 per cent.).

Local tenderness along the course of the sciatic nerve trunk was found only on deep palpation in 83 cases (41.5 per cent.) and was nothing like the exquisite tenderness in what we believe to be early cases of toxic interstitial sciatic neuritis. Local tenderness was not regarded as an important sign. Limitation of straight leg raising was a common finding, being present in 172 instances (86 per cent.). In 81 of the 200 cases (40.5 per cent.) there was muscle wasting in buttock, thigh or calf of the affected limb, usually the calf. Frank weakness of dorsiflexion at the ankle joint was found in only 12 cases (6 per cent.) and frank weakness of plantar flexion at the ankle joint in only 11 (5.5 per cent.).

Changes in objective sensation were noted in some part of the distribution of the affected sciatic nerve in 58 cases (29 per cent.).

The ankle jerks were found to be equal and active in both the affected and non-affected legs in 87 of the 200 cases (43.5 per cent.). The ankle jerk was absent on the affected side in 71 cases (35.5 per cent.). Diminution of the ankle jerk on the affected side was found in 34 cases (17 per cent.), that is to say there was depression of the ankle jerk compared to the normal briskness of the reflex in the opposite unaffected limb. Exaggeration of an ankle jerk on the affected side was found in 8 cases (4 per cent.), i.e., the ankle jerk on the painful limb showed a brisker response than that shown on the opposite unaffected limb.

In only three cases was there any disturbance of function of the bladder and rectal sphincters, and in each instance an extremely large disc was found compressing the cauda equina.

ACCESSORY METHODS OF DIAGNOSIS

Lumbar puncture and Queckenstedt's test were performed in 67 cases, and in only one was there evidence of a partial block in the cerebrospinal fluid pathways. In this case the puncture had been performed below a large herniation at the L4-L5 level, and the protein content of the cerebrospinal fluid was found to be 100 mgm. per 100 c.cm.

In 35 of the 67 cases we found a slight rise in protein content of the cerebrospinal fluid (normal=20 to 35 mgm. per cent.).

In detail, 10 cases had 50 mgm. protein per 100 c.cm.; 8 cases had 60 mgm.; 2 cases had 65 mgm.; 9 cases had 70 mgm.; 2 cases had 80 mgm.; 1 case had 90 mgm.; 2 cases had 100 mgm.; and 1 case had 130 mgm.

In 63 of the 67 cases the white cell count of the cerebrospinal fluid was within normal limits. Only four showed a rise in white cell count, varying from 10 to 60 cells per c.mm. All these four cases proved to have herniated intervertebral discs at operation.

In each case straight skiagrams were made to eliminate such possibilities as tuberculous osteitis, advanced osteoarthritis, secondary carcinomatous metastases and spondylolisthesis. Narrowing of an intervertebral space was seen occasionally, but only when this was very obvious did we regard it as a finding of any particular significance. In fact, preoperatively, narrowing was often noted at the lower space (L5-S1) only to find the herniation at the high (L4-L5) interspace. Air myelography was performed in 47 cases. In our experience it proved of very little value, either in diagnosing the condition or in localizing the site of the herniation. Lipiodol myelograms were made in only 7 cases and then because we were desirous of excluding cauda equina tumours.

OPERATIVE METHODS AND FINDINGS

Of the 200 cases subjected to operation, bilateral laminectomy was performed on 74 (37 per cent.), and hemilaminectomy on 126 (63 per cent.).

In the earlier days a bilateral laminectomy was usually employed as we found that this gave the best exposure. Later, it was found that hemilaminectomy was all that was necessary in the straightforward cases. We found, however, from the final follow-up that bilateral laminectomy gave as good a result as hemilaminectomy. The choice of exposure must be decided at the time of operation and depends upon anatomical and technical conditions. For example, it is wiser to separate the muscle groups conservatively on both sides and to remove one or two spinous processes and laminae rather than to attempt a unilateral exposure if the muscle group on that particular side has to be heavily retracted. Too heavy retraction of a muscle group will damage its nerve supply and lead to muscle weakness and the postoperative complaint of weakness in the back. The principle of the operation is not that of laminectomy but of adequate exposure of a given nerve root from the theca to the intervertebral foramen.

As our experience increased we found that a unilateral approach gave a satisfactory and adequate exposure in nearly all cases.

TYPES OF HERNIATION OF THE NUCLEUS PULPOSUS

Local protuberances due to loose fragments.—Local protuberance of a loose fragment is the most typical type of herniated nucleus pulposus.

At operation a conical mound is seen protruding backwards $\frac{1}{2}$ to 1 cm. from the anterior wall of the canal. Its surface is white and glistening, and it is rubbery in consistency. The involved nerve root is tightly stretched across it but can easily be separated as there are few adhesions. The adjacent plexus of veins and other extradural tissue can readily be swept aside. On making an incision into the capsule the contents of the swelling begin to protrude and can be lifted out in one piece without further dissection. No bleeding occurs when the loose fragment is removed. The cut edges of the capsule fall together and the involved nerve root is left fully mobile. In this type of case we merely remove the loose fragment.

Local protuberances not due to loose fragments.—In these cases an obvious conical mound is encountered, as in the previous type.

On incising the capsule, however, the contents are not free but are firmly attached to its covering and to the tissues more deeply situated in the disc. To effect removal the portion of protruding disc tissue has to be excised by sharp dissection with a tenotomy knife or punched out with punch forceps. The problem is to know how much of the parent disc to remove. Our practice is to ensure that no obvious deeper sequestrum remains and to remove sufficient disc tissue to leave the nerve root free and mobile. Attempts to remove the whole disc are, we believe, futile.

The disintegrated disc.—In this type of case the protuberance is less conical.

The base is broader and the swelling less localized; in other words, the rupture of the annulus has been more extensive. When the disc is incised its contents are found to be loose and granular, apparently being the remains of completely necrotic disc tissue. The contents can be removed with a sharp spoon. In this case we continue with a piecemeal removal until no more tissue can be removed by simple scooping.

The fibrotic nodule.—We have found this type of disc protrusion in coalminers who have suffered from low back pain for many years and who have had severe attacks of sciatica.

A hard grey fibrotic nodule is found beneath the affected nerve root. The nerve root is bound down tightly to the fibrous nodule with strong adhesions, and sharp dissection is necessary to free it. The fibrous nodule has to be removed from the floor of the canal by cutting across its base with a scalpel. The opening into the body of the disc itself is plugged with dense fibrous tissue. All that was done in these cases was to remove the protuberant fibrous nodule and to free the nerve root from its adhesions. We have had excellent results, even though the operation is not so spectacular as in the first type. This is the type of protuberance that can easily be overlooked.

Spontaneous rupture of a herniation.—We believe that some cases of sciatica are temporarily cured as a result of spontaneous rupture of the capsule of the herniation itself, and also that the extruded nuclear material can surround the nerve roots to give rise to reactions that later can cause a recrudescence of the sciatica. In this type of case dense greyish adhesions are found around the nerve roots, and these adhesions are so tough that they can only be removed by sharp dissection.

The intermittent protrusion of a herniated nucleus pulposus.—This type of herniated nucleus pulposus is a sessile type of protrusion and appears only on certain degrees of spinal flexion.

LONG-TERM RESULTS

All 200 patients were kept under close personal review for at least two months following their operations. Only 150 answered our final questionnaire or reported for final examination. Of the 50 uncontacted patients we know that many were abroad. Moreover, several patients have written to us since this inquiry was closed.

In this review of long-term results only the 150 patients who answered our questionnaire will be considered. Ten patients (6.7 per cent.) were reviewed three to six months after operation; 30 (20 per cent.) after six to twelve months; 40 (26.7 per cent.) after one to two years; 50 (33.3 per cent.) after two to three years, and 20 (13.3 per cent.) over three years after operation. Previous to operation every patient, as a result of low backache and sciatica, had been completely incapacitated for all kinds of work, for at least four months; one had been off work for five years.

Length of time before patients returned to employment after operation.—Of the 150 patients who are concerned in this review, 85 were civilians and 65 were in the Services. At the end of the survey we discovered that 144 of our patients were in some form of employment (96 per cent.), and that

only 6 (4 per cent.) were doing no kind of work whatsoever. The patients who returned to work did so, on the average, four months after operation.

Service personnel.—Of the 65 patients who replied to the questionnaire, 20 (30.8 per cent.) were retained in the Service doing their original job; 17 (26.1 per cent.) were retained in the Service on light duties because their original duties were too arduous; 8 (12.3 per cent.) were invalided from the Service and returned to their original civilian employment; 9 (13.8 per cent.) were invalided and returned to a lighter civilian job, as their original civilian employment proved to be too heavy; 2 (3.1 per cent.) who were invalided changed their civilian employment for personal reasons; 2 (3.1 per cent.) who were invalided were not yet working at the time the investigation closed. The remaining 7 (10.8 per cent.) were demobilized in the normal way and returned to their original civilian employment.

From these figures it will be seen that, from the Service point of view, these results are unsatisfactory. Later experience taught us that the Service patients who did well were those who were occupying a high rank, and those who were able to return to a sedentary employment.

Civilian patients.—Of the 85 civilians, 63 returned to their original employment (74.1 per cent.); 14 of these (16.5 per cent.) had to change their employment to a lighter type of work, as their original employment proved to be too heavy; 4 changed their employment for personal reasons. The remaining 4 cases were not yet working at the time the investigation closed. These results are for various reasons much better than those set out in the previous paragraph.

Patients who did not return to work.—Of these six patients, 4 were civilians, the remaining two were from the Services. One of the six patients, a merchant seaman, declared himself to be satisfactorily cured and was merely out of work because he had not yet been found a ship. A second civilian had been satisfactorily relieved by the operation but had had a recurrence of his trouble, as a result of a heavy fall on to his buttocks and back. The other four cases were not totally incapacitated but were men from heavy employment, who felt that they were not yet fit enough to return to arduous work.

RESIDUAL SYMPTOMS

Although a man may return to his work this does not mean that he is entirely symptomless, and not suffering from a considerable amount of discomfort. Each patient was asked to give a frank statement of his post-operative condition, and the results are given in the following table:—

Site of residual pain (if any)	Laminec- tomy (disc found)	Hemi- laminec- tomy (disc found)	Laminec- tomy (no disc found)	Hemi- laminec- tomy (no disc found)	TOTAL
Back	11	6	1	2	(13.3 per cent.) 20
Back and leg. . . .	9	17	4	4	(22.7 per cent.) 34
Leg	3	7	0	0	(6.7 per cent.) 10
No pain in back or leg	23	59	2	2	(57.3 per cent.) 86

In many of the above cases the complaints were minimal; by this is meant that the discomfort did not seriously interfere with the man's mode of life or with his ability to enjoy it. To approach this difficult subject from

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nucleus pulposus and pressure on a posterior nerve root.

In nine patients, extradural root adhesions were found and freed.

In five instances the patients gained satisfactory relief from their pain and in four patients the results were unsatisfactory. On five occasions completely negative explorations were made, no disc being found nor any kind of pathological change in the extradural space. In four of these cases the final result was satisfactory. Judging from these last five cases it might, with reason, be suggested that simple laminectomy would have given satisfactory relief in those cases in which a protuberance pressing on the root was present. Alternatively, it might even be suggested that these few cases prove that low backache and sciatica are not in fact due to the condition that we describe as herniated nucleus pulposus.

CONCLUSIONS

There has been considerable controversy concerning the prevalence, the most common cause, and the prognosis of lumbago and sciatica. This has resulted partly from confusion of thought and statement and partly because different observers unwittingly have given their views of totally different aspects of the subject, believing they were each considering the same problem. To clarify the problem let us consider a million people from one industrial area, and suppose that every new case of low backache and sciatica that occurs within one year reports to a central medical clinic.

First of all let all the patients be treated conservatively by warmth and rest for a few weeks. This will eliminate those who are going to get better quickly by simple means. After this is left what might be described as the second group, and this certainly is a large one, as proved by the fact that from a population of $3\frac{1}{2}$ to 4 million people a thousand cases of intractable low backache and sciatica have been admitted to the Neurosurgical Clinic for investigation, or have been seen in consultation from 1941-47.

Let us now consider that group of cases from which the easily and rapidly curable have been eliminated by the simple measures of rest and warmth. Rectal and vaginal examinations will usually eliminate carcinoma of the rectum or of the cervix, and straight X-rays will as a rule reveal tuberculous osteitis, secondary carcinomatous deposits, or the displacement of spondylolisthesis. Lumbar puncture and Queckenstedt's test usually reveal the presence of a posterior root tumour by the raising of the protein content in the cerebrospinal fluid to above 80 mgm. per cent., and with interference with the hydrodynamics of the cerebrospinal fluid. This group of cases, in which a definite diagnosis can be arrived at by simple investigations, is a small but very important one from the view of treatment and prognosis.

After the elimination of the above types of case we are still left with the third group, in which there is a large residuum of cases in which a precise diagnosis cannot be made by clinical examination or simple investigations. The causes of sciatica in this final group fall into three main classes:—(1) Neuritis; (2) fibromyositis; (3) distortion neuritis due to a herniated nucleus pulposus and allied conditions.

Neuritis.—By sciatic neuritis is meant an inflammatory process within the sheath of the sciatic nerve. This condition, in our experience, is rare and its chief distinguishing clinical feature is the occurrence of severe tenderness

a slightly different angle the patients were asked to state if they considered the operation was worth while.

140 (93.3 per cent.) of the patients replied in the affirmative; 6 (4 per cent.) replied that they had gained no benefit at all and 3 patients did not reply to the question. Also, when asked in another way, 98 (65.4 per cent.) patients stated that they had gained 100 per cent. relief from their pain; 24 (16 per cent.) a 75 to 100 per cent. relief; 19 (12.6 per cent.) a 50 to 75 per cent. relief, whilst 9 (6 per cent.) patients gained no relief at all (0 per cent.). Ninety-five (63.3 per cent.) of our patients stated that they experienced immediate relief from their sciatic pain, when questioned the following morning after operation; 46 (30.7 per cent.) experienced gradual improvement in their pain, and 9 (6 per cent.) did not experience relief at any time.

Nine patients gained no relief from operation.—From these and previous figures it will be seen that three patients who had gained no relief from their operations returned to work. This raises the question of whether or not a large proportion of our patients would not have returned to work even if they had not been operated on. It is almost certain that many of them would have done so. It is, however, our object in this article merely to state the facts and not to compare the results of operative and conservative treatment. Such comparison we hope to make at a later date. What we do know is that many patients of the same period who were treated conservatively are now reporting to us requesting to be operated on because time has not given them satisfactory relief from their low backache and sciatica.

Of the nine patients who did not gain any relief from operation, four had herniated discs removed from the L4-L5 interspace. These patients experienced relief for a short time but within a month or so their pains had returned. In these cases we considered that there had been a recurrence of the herniation which had been previously removed. In two patients herniations were removed from the lower interspace. These patients did not gain relief from their pain at any time, and it is possible, and even probable, that in both cases there was a second disc at the higher interspace which had not been explored at the original operation. In one case a disc was found and apparently satisfactorily removed, so far as can be judged. This patient was relieved from his leg pain but was left with crippling backache, and the operation was of no therapeutic value. In one patient no disc was found but extradural adhesions were present surrounding the nerve root. In the ninth case a definite herniation was found at the L5-S1 level, but here also there were considerable extradural root adhesions.

PATIENTS WITH NO HERNIATED NUCLEUS PULPOSUS

In our series of 200 laminectomies, carried out for low backache and sciatica, a herniated nucleus pulposus was not found on 22 occasions. In the present long-term review of 150 laminectomies there were 15 "negative explorations" for herniated nucleus pulposus. On one occasion a tuberculoma was found which occupied the same position as a herniated nucleus pulposus and was more or less of the same shape.

When the capsule was opened, necrotic matter exuded from the protuberance, which on histological examination proved to be tuberculous. The operation gave the man immediate relief from a very severe sciatica. After a prolonged rest in bed he made a complete and satisfactory recovery. Preoperatively, there was no radiological evidence of tuberculous osteitis in the lumbar spine. Clinically, the signs and symptoms were indistinguishable from those which are aroused by a herniated

PHYSIOLOGICAL AND MEDICAL PRINCIPLES OF TRAINING

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By physical training is meant the building up of the body. This may be general building-up for all purposes of health, efficiency and enjoyment of life; it may be special building-up for a group of purposes, as in training for war or sport; or it may be specialized building-up for one specific purpose, as in training for gun manhandling or track athletics. Whatever the connotation applied the same general principles hold. It involves the study and handling of the whole individual twenty-four hours a day and seven days a week for a prolonged period running into months and years. This naturally includes considerable detail, differing with individuals and circumstances, but once these principles are understood their detailed application is largely a matter of common sense, in which is included ability to handle persons.

First to be faced is the fact that man's body and mind cannot be separated either from one another or from his surroundings. The "psychosomatic medicine" of recent emphasis has been known and admitted under other names for many years. More recently detailed statistical work on the measurement of the two, such as that of Sheldon (1940, 1942), has stressed their interrelationship. Which is the more important in training may well be debated, but that both must be considered is obvious. Physique based on anatomical structure limiting physiological function would appear to be the first necessity. Physical training implies a full knowledge of the body and its working; this includes body mechanics, which is the mechanical correlation of the various systems of the body with special reference to the skeletal, muscular and nervous systems, and to the mechanical effects on the internal organs of the other systems. This is well- if rather over-emphasized by Goldthwaite *et al.* (1941). It would seem to be the basic requisite on which is grafted the applied physiology of training, the application of knowledge of the normal living functions. This was well reviewed by Steinhäus (1933). More recently the two together have been covered comprehensively, though less convincingly, by Jokl (1941), who to some extent essays to cover the psychological side. The importance of this can scarcely be overrated, but its complexity is great. Intellectual capacity and emotional stability are definite factors in training. Ultimately the whole question of motivation arises and may well be the final limiting factor, and a goal should be set to provide an incentive.

BUILDING-UP THE GENERAL HEALTH

The raising of the general health should first be briefly considered. For

along a length of the sciatic nerve to the lightest palpation; a degree of tenderness which rarely occurs in any of the other forms of sciatica. Also, the pain of a true neuritis in the early stages is so severe that the patient is completely incapacitated and has to remain in bed.

Fibromyositis.—As a large nerve passes along or through a large muscle group it forms for itself a channel, the walls of which are so smooth and so frictionless that the nerve is virtually surrounded by a synovial sheath. As a result of some pathological process, adhesions can form between the fibrous sheath of the nerve and the lining membrane of its muscular channel. Thus, instead of the nerve being able to slide freely with the movements of the limb it is tethered and subject to traction when the limb is put on a stretch. Probably the pain of fibromyositis is due, in a large number of cases, to this condition of perineuritis.

Herniated nucleus pulposus.—Although it is doubtful whether there is any clinical picture that is absolutely characteristic of a herniated nucleus pulposus, it is true that when every pathological lesion that is capable of demonstration has been eliminated by suitable investigations the chances are that, in nine cases out of ten, the causative lesion of the low backache and sciatica will prove to be a herniated nucleus pulposus.

Principles of treatment.—When carrying out a laminectomy for the relief of low backache and sciatica the guiding surgical principle should be exploration of the suspected nerve root in the whole of its intraspinal course, from the side of the theca to its exit at the intervertebral foramen. With practice, this can be done in most cases by means of a partial hemilaminectomy. Any sacrifice, however, of adequate exposure of the nerve root, to a fetish for shortening an incision or minimizing a laminar removal, is unwise. We have always concentrated on gentle handling of the tissues and avoidance of heavy retraction.

The alternative to surgical removal of a herniated nucleus pulposus which is causing low backache and sciatica, is adequate rest. By this is meant complete rest in bed, so that the weight of the body above the affected intervertebral disc is transmitted directly to the bed and not through the disc itself. Sitting up in bed is therefore not permissible; on the other hand, the head and neck may be made comfortable with a couple of pillows. It is too irksome to keep the patient entirely on his back, and little harm is done if he is allowed to roll on to his side or on to his face. He should not be allowed to get up to go to the lavatory or to sit up when his bed is being made. Three weeks is the minimal period a patient should be confined to bed and, if possible, he should be kept there for as long as is reasonably necessary to give him relief. Probably if more patients were so treated in the early stages of their illness, far fewer would finally come to operation.

We would like to express our appreciation of the criticism and guidance of Dr. E. A. Carmichael, Professor Sir Geoffrey Jefferson and the late Dr. George Riddoch in the production of this article; also our thanks to Miss Robson and Miss Curtis for all the hard work they have done in producing the figures for the follow-up.

functions more efficiently. In this connexion in training, weight should be regularly checked; it is probably the best easily measured objective indication of physical health. Slight daily variations of weight are mainly due to fluid loss and should be rapidly regained. The average person probably takes insufficient fluid. In training so much is lost in sweat that it must be made good. The addition of extra fluid to a training diet is usually desirable. Excess with food should be avoided but more might be drunk between meals. Water is the essential physiological drink, but milk, tea, coffee and cocoa in moderation are all desirable parts of a sane and balanced diet. Salted water in summer training reduces the likelihood of cramp. The proper distribution of food throughout the day is of importance. After the night's rest, the body stores are at their lowest ebb. To replenish them a substantial breakfast is necessary. The rest of the day requires smaller, more frequent additions to the stores. But, ideally, the last meal of the evening should be a full one if the body is to be given the means of repair and building during sleep.

Sleep and rest.—Time and opportunity for the food to be properly absorbed and used by the body are the next requisites in training. Their importance is frequently not sufficiently recognized. By rest we mean all degrees of absence of work, from sleep in the lying position to relaxation in the upright. Sleep is nature's chance to re-form the body tissues after the breaking down of the day's activities. It allows the blood time and opportunity to bring to those tissues food for body building and for repair. The blood must also remove waste products for disposal and excretion through lung, bowel, bladder and skin. This means that even during sleep the body is doing internal work. It is using up its stores of food and water, and requires a full supply of oxygen. It is obvious therefore that the body is at its lowest physical potential when the individual first rises from bed in the morning. For this reason vigorous bodily exercise before breakfast should be deprecated.

How much sleep and rest are necessary is largely an individual matter, and depends partly upon the training as well as upon the age. Eight hours' sleep a night is a good average. Even a little more may be desirable, but as in all good things excess is bad. Rest, however, probably does most good if plenty of available fresh air ensures oxygenation of the blood and stimulation of the skin. Rest periods during the day should be fitted in with the active periods of physical work: "Activity and rest, alternating and in due relation to each other, form the physiological basis of, and key to, health in man . . ." (Hilton, 1863).

Physical exercise is what comes uppermost to the mind in training. By this we imply the use of muscles more strenuously and for longer periods than they are normally used in the ordinary regime of a sedentary life. All exercise should be governed by the use of moderation, progression and regularity. Its purpose is the threefold one of developing endurance,

first-class performances in any sport both body and mind must be fit. The mind should be free from worry; judgment, will-power and the ability to concentrate should be developed. Each system of the body, skeletal, muscular, circulatory, respiratory, digestive and nervous, should be functioning at its optimum. The relative importance of congenital and acquired properties will not be discussed here, although longer observation in training leads me increasingly to the conclusion reached in medicine by Julius Bauer (1943), who stresses the inborn constitution. In the case of the individual in training this can best be assessed by a periodic medical overhaul, whilst the acquired properties can be measured concomitantly by watching the effect of common-sense advice. This advice concerns the correct handling of the three main components of body building, and of the other less important but desirable adjuvants. These three are food and drink, sleep and relaxation, and physical exercise and work. They might be considered as the main ingredients in a medical prescription with additions to taste! These additions include fresh air and sunshine, alcohol and tobacco, baths and massage, clothing and shoes.

Diet.—The body lives and grows by means of the food put into it; it works by virtue of the energy released when that food is broken down chemically and later partly rebuilt by combination with oxygen. This stresses the obvious importance of food and the working of the whole of the digestive system. In training there are two aspects to be considered—the physiological, which may be thought of as carbohydrates, proteins, fats, vitamins, minerals and water, and largely measured in calories, and the psychological, which is more indefinite but includes the look, feel, taste and smell as well as the bulk. In peace time, viewed physiologically, these usually received unnecessary attention. Although stress might have been laid on one or two details, such as fresh fruit and vegetables and extra milk and butter, the usual meals of good plain food obtained in the average home or boarding school were sufficient training diet for the normal person. To-day, diet needs more consideration than is possible here. Food serves the two main purposes of energy production and replacement of worn-out body tissues. Appetite, guided by common sense and moderation, dictates both quantity and quality. Indigestible foods and overeating are obviously harmful, whilst the regular spacing of meals and the avoidance of strenuous exercise immediately before or after, as well as the habit of eating slowly and chewing well, are of more importance than the food itself.

The immediate effect of exercise is the drawing away of blood from the digestive tract, with such results as a diminution of gastric activity (Hillebrandt *et al.*, 1935) and the depletion of the accumulated store of available food in muscle and liver. As a general rule physical training should not take place within approximately half an hour before, and one hour after, a heavy meal. The ultimate effect is that the body demands more food and the digestive system, in common with all the body systems,

Hygiene.—General cleanliness is desirable for good health. Morning baths, warm showers after exercise and warm baths in the evening have their place according to personal taste, but in general too hot baths are enervating. Massage is an overrated means to physical fitness. In moderation and in the hands of an expert, it is a useful adjunct, aiding relaxation and rest. The heavy "rubbing" with foul-smelling liniments so frequently administered by enthusiastic "trainers" is harmful. More good will come from judicious warming up before and cooling down after the day's main exercise. I have found that a short relaxed swim in warm baths immediately after a day's training served better as self-massage; but hard experience taught that it must follow and never precede strenuous exercise on a hard surface. Massage after injury is a different matter, and should be used under medical advice; this I have previously discussed (Lovelock, 1947).

Finally, attention should be paid to such details as light warm clothing and comfortable shoes. Both dentist and doctor should be visited for periodic overhauls. Defæcation should be regular, but introspective "bowel consciousness" should be discouraged. Ailments and injuries, few in a fit man, should receive early and drastic treatment to avoid training delays.

BASIC FACTORS IN SPECIFIC TRAINING

Having dealt with the main requirements for the preliminary raising of general health, something will next be said of the special building-up for a group of purposes. These principles apply to all physical training, where the aim is not only to build up the body but also to develop further the definite properties of strength, endurance and skill.

Strength is largely a property of the skeleton and muscles and their connecting tissues. One effect of exercise on the skeleton is to strengthen the bony tissue and accustom it to strain. The main effect is on the moveable joints where increased mobility follows moderate use, and increased stability comes with combined increase of muscle power and control. Increase of strength is associated also with hypertrophy of muscle, the fibres of which gain in size and strength from the food used. The more they are used the more food is brought to them, with resultant increase in growth. Strengthening exercises are those which require maximum slow contraction of muscle, frequently against resistance. The resistance may be that of gravity or of an outside agent such as a tennis racquet or a 16 lb. weight.

Endurance, or the postponement of fatigue, is a measure of the body's ability to balance catabolic with appropriate anabolic processes. Primarily, this means a sufficient supply of oxygen, and secondarily, a food supply. Thus the coordinated work of the circulatory, respiratory and alimentary systems is of main importance here, this coordination being due to the nervous system, particularly the autonomic portion, and the endocrine system. Muscular exercise requires various adjustments of the circulation so that more blood shall flow to the working muscles. Extra blood will be

strength and skill; qualities which, though concerning all the tissues of the body, may be considered to derive their main properties from different systems. These will be discussed in more detail later. Before any strenuous exercise is begun, skeletal muscular circulation should be increased by mild general bodily activity (limbering up). Similarly, at the end of strenuous exercise, all muscular activity should not cease suddenly; circulation should still be encouraged to remove the end-products of muscular contraction (limbering down). All exercise is not strenuous enough to require this. Moderate exercise of all types plays an important part in building-up the whole body to function efficiently before any one part can give of its best. All-round development of the body by moderate participation in games and exercise, whether team or individual, competitive or otherwise, must precede any form of special training. Football, cricket, rugger, hockey, tennis, squash, gymnastics and swimming are all enjoyable exercises, whilst the value of long walks and steady jogging can scarcely be over-estimated. Swimming in moderation is particularly valuable in acquiring the relaxation and rhythm necessary for many athletic events.

This brings the subdivision of games and sports into what has always appeared to me a fundamental grouping, the larger group of asymmetrical ones and a smaller symmetrical group. Both have their constituent sports differing in degree of coordination and relaxation. For general physical fitness all forms of exercise should be used; as training progresses, the field of selection should be narrowed to that of the type into which the chosen sport falls. Neglect of this grouping in the later stages of training is one of the common causes of failure and of muscle injury. In track athletics special mention may be made of the symmetrical, relaxed, coordinated group, of which walking, running, gymnastics and swimming form the main items. Dancing is a good exercise and excellent mental relaxation, but the late hours with concomitant alcohol and tobacco have to be considered.

Fresh air and sunshine are acknowledged accessories in gaining all-round physical health. Their beneficial properties are well known. Apart from the necessary blood oxygenation and the desirable actinic or chemical effect of ultra-violet light on the skin, there are the less measurable good effects, partly physiological, partly psychological, of the stimulation of the skin mechanically by wind and thermally by sun, of the retina by light and of the olfactory mucous membrane by pleasant odours.

Alcohol and tobacco are equally accepted as detrimental to physical health. They are generally agreed to be mild physical poisons. The effect of smoking on endurance performances was observed in nearly 2,500 men at the Army School of Physical Training at Aldershot over a period of seven years. Although the maintenance of adequate control groups was difficult, it appeared that performances of endurance were more adversely affected than were those of speed. In general, however, although both alcohol and tobacco encourage mental relaxation, the ideal in training is abstinence.

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pumped out to the periphery more rapidly by the heart, which will have increased work to do both there and in pumping the blood through the lungs. The ultimate effect of exercise is that the whole circulatory system is trained for greater work. The immediate effect of exercise on respiration, however, is seen in external breathing; this is but the mirror of the internal respiratory processes. There, working in collaboration with the circulation various complicated processes appear to act together to speed up the rate of the availability of the blood-borne oxygen to the muscle cells. Oxygen transport is possibly aided by lactic acid buffering ability; improvements in this property have been observed in the increased alkali reserve and called a form of chemical training. The immediate and ultimate effects of exercise in the alimentary system have already been mentioned. Endurance training entails prolonged exertion without recovery periods of rest; this takes the form particularly of long walks and long runs.

Skill is largely a matter of the control of the central nervous system over the skeletal muscles. Training facilitates the passage of messages to muscles, as well as the return of messages from them. This means more efficient action, for the muscle groups will coordinate better in their work, making for simpler and more economical movements. Undoubtedly the greatest and most lasting changes which training induces take place in the nervous system, namely, changes in behaviour. Among these changes the most obvious are those which manifest themselves in "muscle learnings" or improved coordination. Perfection of movement is the most prominent result of training as well as the most specific. Endurance may be developed by boxing, swimming or running, but the finesse of boxing can be perfected only by the practice of germane movements. A most important by-product of the development of skill is the economy of effort which the more purposeful use of the muscles entails. This reduces the total load and at once postpones fatigue. A large fraction of the trained state is probably due to the establishment of conditioned reflexes involving adjustments, through the autonomic nervous system. This conception includes such reflexes as the acceleration of the heart and respiratory rate in anticipation or at the beginning of any contest. Training for skill requires the use of any movement of dexterity with the ultimate acquisition of precision, and takes the form of movements allied in nature to that being trained for. This merely emphasizes the grouping into symmetrical and asymmetrical already mentioned.

TRAINING FOR TRACK ATHLETICS

The general principles of special training for sport having been discussed largely from a physiological angle, the specialized training exemplified by track athletics, especially the middle distances, will next be considered in more detail. Here a similar interlocked grouping may be used, although the desired qualities will be called stamina, speed and style, to which judgment

may be added rather as an intellectual than as a physical requirement.

Stamina, although usually associated mainly with middle and long distance running, is no less necessary for sprinters and field event men. The former need it to last out even 100 and 220 yards, whilst heats and finals or several races in one day make heavier demands. One of the main faults with British sprinters in the past has been their failure to realize the essential need of this vital factor. Field men also require it to give continued strength and suppleness to their movements. Stamina is the basis on which speed and style must be founded. Ability to move fast and technical perfection in movement are useless unless the athlete is able to get through heats and preliminaries in a fit state. Stamina is obtained in two ways: by the general healthy living already outlined and by long steady walks, gentle jogging and striding, the distance and pace varying according to the special event; but the distance should be greater than that required in competition and the pace slower. For example, in middle distance training, the length may vary from one to four miles, depending upon the pace; both pace and distance should increase with increasing fitness. Here I wish again to emphasize that throughout the training period, as well as at the beginning, an essential part of all work should be several laps of preliminary jogging and gentle striding in order to warm up the body, and a few more laps at the end to allow it to cool down gradually. Stamina should be kept in mind as the basis of middle-distance training, and even when speed is being concentrated on, a definite part of the week's exercise should be allocated to long, stamina-producing work. Adequate clothing and comfortable shoes should be worn.

Speed is the essential ingredient in sprinting; but other runners need it in degree varying with the distance. It is obtained partly by slow work to strengthen the muscles and educate them in coordinated movement, but more obviously by faster work with hard bursts to accustom those muscles to contract and relax maximally at high speed. It must not be thought of until the body is generally fit and sufficient stamina gained. After the first few weeks of gradually increasing track work, striding finishes should be practised, and later short sharp bursts mixed in with the usual striding. It must be stressed that training conditions should approximate as closely as possible to those of competition, and the type of speed required in racing should be aimed at in training. Thus it is useless and even harmful for middle- and long-distance men to work with sprinters in sharp bursts from holes. Their fast work should always be taken in the middle of steady striding. To avoid strains and pulled muscles care must be taken that the body is fully prepared, with the circulation well established, the muscles warmed and the joints thoroughly loosened. Similarly, abrupt stops should be replaced by steadier slowing down.

Style is the most controversial and complicated of the four factors; but if the principles are understood it can be greatly simplified. It may be summarized as ease and economy of effort when every muscle is actively

directed towards one end and all movements are aimed in the one direction. It embodies many points, but is most easily considered under its main physiological parts. A simple subdivision is into five: head poise and body balance, foot and leg action, arm and shoulder action, limb coordination and rhythm, including that of breathing and relaxation.

The poise of the head controls the balance of the body. It should be held steadily in alignment with the trunk, chin neither tucked in nor stuck out. Neck muscles should be relaxed with eyes looking ahead to a point 20 to 30 yards on the ground. Chest and hips should be square to the front; the line from head to heel should be straight. At first a conscious effort to maintain this alignment may be necessary, as with the assumption of any easy economical posture; in time the balance will come, and with it greater relaxation and ease of movement. In running, as in any body movement, the essential thing is the shifting forward of the centre of gravity of the body, controlled by the head; falling forward is then immediately prevented by the interposition of the legs.

Leg action is the main dynamic force in running. The legs are the driving force behind the body as well as the pulling force in front of it, but essentially they are the supporting power beneath it. It must be stressed that as the aim is to shift the body as quickly as possible in one definite direction, movement away from this straight line is wasted, except in so far as it may aid balance. Toes should be pointed straight ahead and knees lifted forwards; a bounding action, the usual accompaniment of too long striding, should be avoided as the body weight is moved unnecessarily upwards. The head and body should be kept on a level plane of movement with the legs moving smoothly beneath. In practice this is best ensured by concentrating on pulling the knee-cap forwards with the thigh muscles; concentration on the lower leg is not desirable, as better relaxation is obtained if it be ignored. On landing, the knee is kept slightly bent, but as the superimposed body weight passes forward the rear leg straightens out into a drive.

Arm action is relatively unimportant. The dual function is to assist the body balance, and to control the speed of leg action. If the body balance is sound, their aid as balancing mechanisms should be minimal. Excess arm action in distance work is an admission of poor body balance. In sprinting, on the other hand, vigorous arm movements hasten the more heavily muscled and laden legs. Muscles of shoulders and hands should be relaxed and details of height of arm carriage and direction of motion are secondary to the primary principles of economy and comfort.

Limb coordination and rhythm are automatic to maintain body balance and ensure easy movement. Change or break of rhythm leads to less efficiency and greater fatigue. Even respiration is bound to follow an automatic rhythmic rate set up by the limb movements. As the product of depth and rate determines the air intake, which is an automatic demand of the internal tissue respiration, its regulation should not be interfered with by voluntary.

effort. Particularly in sprinting no artificial holding of the breath should be practised.

Relaxation is the secret of muscular economy. Postural balance should be such that muscles controlling the body position are doing minimal work, whilst no muscle group not actively helping to move the body in the required direction should be fully contracted. Contraction follows relaxation only when necessary work is being done. Increase of relaxation takes practice and concentration; isolated limb action in sectional practice is a great help; this is furthered by slow running during which every effort is made to let all parts flop loosely.

In summarizing these details of style, running may be considered as a rapid forward transition of the centre of gravity of the body in which the various individual organs all play a part. The head is the main factor with its incorporated semicircular canals and eyes primarily controlling all movement through the central nervous system. The body, with forward slant and easy straight alignment from head to heels, is prevented from falling forwards by the underlying legs. These also actively propel it and draw it onwards. The arms are used minimally, consistent with body balance and limb coordination. All parts work rhythmically, and the relaxation of antagonists ensures the efficient use of all prime movers.

Finally, a word about *judgment*, the prime factor in long distance work when the aim is to spread the energy output most economically. It implies concentration on any trained movement. In practice it is obtained by continual observation and measurement. Sprinters must gauge the pace in heats and finals; distance men depend upon it for tactics as well as for economy, and field men judge run-up, release and trajectory. All these must be practised in training, in which for track athletes periodic time trials, not necessarily at full speed, are the best means of its acquisition. Practice and concentration alone will bring this knowledge and with it the self-confidence and increased ability of an experienced athlete.

The discussion of these general principles should simplify the understanding of training and of athletic injuries, the treatment of which is simple when the underlying physiology and pathology are known.

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directed towards one end and all movements are aimed in the one direction. It embodies many points, but is most easily considered under its main physiological parts. A simple subdivision is into five: head poise and body balance, foot and leg action, arm and shoulder action, limb coordination and rhythm, including that of breathing and relaxation.

The poise of the head controls the balance of the body. It should be held steadily in alignment with the trunk, chin neither tucked in nor stuck out. Neck muscles should be relaxed with eyes looking ahead to a point 20 to 30 yards on the ground. Chest and hips should be square to the front; the line from head to heel should be straight. At first a conscious effort to maintain this alignment may be necessary, as with the assumption of any easy economical posture; in time the balance will come, and with it greater relaxation and ease of movement. In running, as in any body movement, the essential thing is the shifting forward of the centre of gravity of the body, controlled by the head; falling forward is then immediately prevented by the interposition of the legs.

Leg action is the main dynamic force in running. The legs are the driving force behind the body as well as the pulling force in front of it, but essentially they are the supporting power beneath it. It must be stressed that as the aim is to shift the body as quickly as possible in one definite direction, movement away from this straight line is wasted, except in so far as it may aid balance. Toes should be pointed straight ahead and knees lifted forwards; a bounding action, the usual accompaniment of too long striding, should be avoided as the body weight is moved unnecessarily upwards. The head and body should be kept on a level plane of movement with the legs moving smoothly beneath. In practice this is best ensured by concentrating on pulling the knee-cap forwards with the thigh muscles; concentration on the lower leg is not desirable, as better relaxation is obtained if it be ignored. On landing, the knee is kept slightly bent, but as the superimposed body weight passes forward the rear leg straightens out into a drive.

Arm action is relatively unimportant. The dual function is to assist the body balance, and to control the speed of leg action. If the body balance is sound, their aid as balancing mechanisms should be minimal. Excess arm action in distance work is an admission of poor body balance. In sprinting, on the other hand, vigorous arm movements hasten the more heavily muscled and laden legs. Muscles of shoulders and hands should be relaxed and details of height of arm carriage and direction of motion are secondary to the primary principles of economy and comfort.

Limb coordination and rhythm are automatic to maintain body balance and ensure easy movement. Change or break of rhythm leads to less efficiency and greater fatigue. Even respiration is bound to follow an automatic rhythmic rate set up by the limb movements. As the product of depth and rate determines the air intake, which is an automatic demand of the internal tissue respiration, its regulation should not be interfered with by voluntary.

to notice only a few yards away a blatant neon sign which informs the people of Rochester that "CHIROPRACTIC GETS SICK PEOPLE WELL".

At a later hour that morning I went and introduced myself at the Clinic in the dual capacity of "visiting physician" and patient. As one of the innumerable medical visitors who crowd to this spot from Reykjavik, Santiago, Hongkong, Paris, and so on, I was received at once by the charming lady secretary whose sole function appears to be to explain what the Mayo Clinic has to offer to its visitors. Its library, museums, clinical meetings and so on were at my disposal; I was cordially invited to a weekly buffet supper with members of the staff, and I was able each day to take my choice from a large printed sheet listing the two hundred or so operations to be performed at the four associated hospitals. Everyone was only too pleased I had come and hoped I would stay for as long as I chose.

As a patient I offered myself to the Mayo Clinic for routine overhaul. The Mayo Clinic was apparently delighted to accommodate me and arranged my series of investigations far more quickly than if I had been a mere layman. This experience is one I would recommend to other medical visitors to the Clinic. It gives one an insight not otherwise attained into the smooth working of a superb organization which combines high technical efficiency with large-scale, one might almost say mass-production, methods. First there was a preliminary interview with detailed history taking and clinical examination. Then I was given a list of eight or nine appointments, for each of which there was a coloured envelope on which were clear printed instructions. These envelopes were to be presented at appropriate departments in the course of the next four or five days. The number of fellow patients attending for these investigations was always very large, but the organization was such that it was rarely necessary to wait for more than a few minutes. Those few minutes were always passed in luxurious surroundings and gave one a chance to admire the internal decorations of the Clinic building, which made me think of the palaces of Maharajas I had seen in India.

The occasion when I attended for a blood count was typical:—

After the usual ten minutes in a comfortable armchair I was summoned by one of the innumerable young lady receptionists to enter the laboratory specializing in blood counts. A specimen was quickly removed from the lobe of an ear by a pair of young lady technicians, one using the needle and the other the pipette, and it was at once passed on to a long row of giggling but presumably competent young ladies seated at a row of microscopes. As I came away holding a gauze swab to my ear it seemed typical of the place that an elegant receptacle had been placed at the ideal spot just where one would be most likely to tire of, and wish to dispose of, one's gauze swab.

Alas though, even in the most efficient organization the human element may fail, and when the moment came at which, in the most perfectly designed little cubicle, I was expected to produce a fresh faecal specimen I failed and was overcome with shame. I felt that somehow I had let the

COMING HOME ACROSS THE STATES

By HANDLEY T. LAYCOCK, M.B., F.R.C.S.

To most Englishmen the fantastic silhouette of New York is their first view of America. Mine was the Californian coast and the gracious outline of the Golden Gate bridge. I had crossed from Shanghai, with fleeting glimpses of Japan and Hawaii, on a former American transport, the standard of comfort on which was, in spite of two years of so-called peace, surprisingly low. We left her without regrets. My fellow passengers were almost all either displaced persons of European origin, glad to leave Shanghai for ever and all desperately hoping for that panacea of all displaced persons, American citizenship, or students from the Philippines and China on their way to colleges in the States. There were thirty or forty Chinese doctors on their way to postgraduate study in the medical schools of America.

I found the sudden impact of American culture in San Francisco exhilarating and bewildering, and in the few days I spent there I only began to explore its wonders. Here, as everywhere in this my first experience of America, I met with and was embarrassed by the lavish hospitality of total strangers.

Eager to miss nothing of the natural wonders of the West and to avail myself of all the advice given me by well-meaning people who knew the National parks and monuments so liberally scattered over the continent, I had reached California with a dozen prospective routes in mind for crossing America. However, the decision was made for me by the Greyhound bus company's persuasive agent who met my boat and who had no difficulty in picking out the ideal itinerary for me. I soon found myself with an enormously elongated bus ticket which would take me in easy stages all the way to Halifax. It cost me no more than about £30 for a journey three times the distance from Calais to Constantinople.

THE MAYO CLINIC

My first medical objective was the Mayo Clinic, but before I got there I had a vivid but all too kaleidoscopic experience of the *Sequoia* forests and coast of California, the glories of early autumn in British Columbia and the Canadian Rockies, and the vast expanse of prairie that brought my bus to Winnipeg. I have nothing but praise for the long-distance Greyhound buses and, if one is in a hurry as I was, as soon as we had passed the scenic splendours of the mountains they can certainly "step on it". From Calgary to Minneapolis I travelled all day and all night and covered the 1,400 miles in 40 hours. And so at 3 o'clock one morning I found myself alighting in Rochester, Minnesota. Even at that hour one realized at once that the city was dominated by the Mayo Clinic, the summit of whose high tower carries a great revolving beacon like a lighthouse. I was amused

extraordinary specimen to be photographed at once, but he had scarcely given this order when the junior nurse who was carrying it away upset the basin and dropped it. It burst and scattered several gallons of dark brown slime all over the theatre. With great self-control the surgeon merely cancelled his order to the photographer!

Nearly everybody and everything in Rochester seems to be in some way connected with the Clinic. The innumerable hotels cater for its patients, and one never gets away from them in the city's restaurants. If one cares to listen to the conversation of one's neighbours it is nearly always of a medical nature: "Perhaps physiotherapy would help"—"You see he thinks he has got cancer so they have given him a complete overhaul and it has cost him \$100"—"Good gracious! I hope mine isn't going to cost that much"—"They removed one of her kidneys and now they are going to remove the other one and replace it with some sort of artificial kidney", and so on. This last extraordinary statement was perhaps related to a case in which considerable interest was being taken when I was at Rochester. Going to see her was popularly described as "going to see the artificial kidney".

A young woman at a hospital several hundred miles away had been given a transfusion of incompatible blood and had been brought to Rochester as an emergency with complete suppression of urine and advanced uræmia. When I saw her she was being treated with continuous peritoneal lavage, using a modified Ringer's solution as the irrigating fluid. This was running in slowly through a rubber tube inserted below the right costal margin and being sucked off again through another tube in the pelvis. Her general condition was improving and her blood urea was steadily falling. As a prophylactic against peritonitis she was being given three-hourly injections of penicillin and streptomycin.

The museum.—One of the features, one might almost say the curiosities, of Rochester is the museum conspicuously situated in the square opposite to the entrance to the Clinic. This is open daily for the instruction of the public, which means in practice the vast number of visiting patients. They are shown a remarkable series of wax models illustrating the essentials of modern medical and surgical practice. If you have come to Rochester suffering from a disease for which surgical treatment is recommended you are encouraged to go and study its nature and the methods of attacking it set out so clearly and so attractively in this museum.

CHICAGO

After Rochester I went on to Chicago and attempted too much in one week by trying to see its museums and art galleries as well as its hospitals. Among the latter I selected the Cook County Hospital and the Wesley Memorial Hospital, which cater for the lowest and highest social strata respectively.

At the *Cook County Hospital* many of the patients are negroes and the majority are non-paying. Many of the wards were very crowded and, particularly in the maternity section, beds had overflowed and occupied much of the corridor space. Quite a series of œsophageal resections had been done on the morning of my visit and about half the cases in the surgical recovery ward seemed to be recovering from this operation. In

Mayo Clinic down. The young lady whose function it was to attend to these specimens was gracious to me and said that I might come back and try again in half an hour's time !

Surgery at St. Mary's Hospital.—As a surgical visitor I soon found that I could usually make the best use of my time at St. Mary's Hospital. The surgical menu was always good and there are twelve theatres to choose from. The nature of the operation in progress in each is indicated by a lighted number flashed on to a screen. If one wishes to wait for a particular operation one can sit in comfort watching for the appropriate number to be flashed on this screen. An iced coca-cola machine provides liquid refreshment for those so engaged, and anyone interested in surgical pathology can stroll around and admire a wonderful collection of wax models.

The large number of surgical visitors makes it impracticable to admit them to the floor of the theatres, and to some extent there is a feeling of being kept at arm's length. This was compensated for by using prismatic binoculars and by the readiness of the average American surgeon to employ an elaborate surgical technique and to keep up an entertaining running commentary on it at the same time. Most of all I enjoyed watching Dr. Clagett. In the course of my first week I saw him resect two coarctations of the aorta, tie a patent ductus arteriosus, perform Blalock's operation, and do a whole series of lobectomies, gastric resections, and so forth. That one surgeon can get through a really astonishingly long list of major cases at one session is made possible by a smoothly running organization that never fails to produce the right patient at the right time, and by the method of using two theatres and two teams of assistants who make and close the incisions for each senior surgeon. Routine anæsthetics are, as is well known, given by whole-time nurse anæsthetists. The Mayo Clinic conception of the anæsthetic specialist is someone who performs elaborate local nerve blocks and gives intravenous therapy, and at the same time supervises in a general kind of way the inhalation anæsthetics being given by perhaps half a dozen nurses.

Some things in the operating theatres surprised me. One was a rather casual attitude towards skin preparation. For example, I saw a woman arrive in the theatre for a colon resection and undergo what was obviously her first skin preparation immediately before the operation began. Another thing was that I saw no evidence of a ritual for counting gauze swabs, although it was pointed out that every piece of gauze used had woven into it a few threads of a radio-opaque material by which its presence could be detected if it should have the misfortune to be left inside. Only once did I see anything go really wrong at an operation:—

The patient was a young man with an enormous cystic swelling in his upper abdomen, presumably a pancreatic cyst. When the abdomen was opened it turned out to be a huge splenic cyst, larger than anything anyone present had ever seen. Splenectomy was quickly carried out and the spleen, which must have weighed 30 to 40 lb., was removed intact. The operating surgeon gave instructions for this

extraordinary specimen to be photographed at once, but he had scarcely given this order when the junior nurse who was carrying it away upset the basin and dropped it. It burst and scattered several gallons of dark brown slime all over the theatre. With great self-control the surgeon merely cancelled his order to the photographer!

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some of the chronic wards I was shown the Striker rotating frame for turning "spinal" cases: it looked like an answer to the orthopaedic sister's prayer.

The *Wesley Memorial Hospital* demonstrates how well the skyscraper adapts itself to the purposes of a hospital. With the main axis of the building vertical rather than horizontal the patients are accommodated in single rooms or small wards, none of which are more than a few yards from the central elevators, which convey personnel, patients, beds, supplies, and the like, from one level to another with far less effort than in the more conventional type of hospital with its elongated wards and long draughty corridors. The nurses simply push the patient in his bed in and out of the elevator, and the elevator does the rest.

TORONTO

From Chicago I went on to Toronto and spent a very pleasant week at the hospitals connected with the *University Medical School*. Here I saw the most drastic pneumonectomy I have ever seen. The left lung was removed for bronchial carcinoma, and a large part of the left side of the diaphragm and pericardium were removed with it. The surgeon said that he would not have hesitated to remove a piece of the left auricle if that also had been involved.

NEW YORK AND BOSTON

Then came New York, which of course beggars description. I had only time for one hospital and chose the New York Hospital (Cornell University), another supreme example of the skyscraper-hospital. I walked in on a urological morning. A senior member of the staff was showing his assistants how to do prostatectomies by various techniques. One of them told me that in one morning he had removed the prostate by the suprapubic, retropubic, perineal and transurethral routes, an achievement which has, I imagine, not been claimed outside America! My hosts seemed pleased to be able to show me their way of doing the retropubic operation, which they said they had recently been taught by my fellow-countryman, Mr. Millin. At the recent surgical congress television machinery had been installed in the theatres of this hospital to enable large audiences to watch operations. As a stunt this may have been spectacular, but for purposes of serious teaching it is considered very inferior to the ciné film. The film has the advantage of natural colour and, if anything should go wrong, judicious editing can exclude it from the film but not from the television demonstration, which, like the traditional camera, "cannot lie".

After my all too brief visit to New York I went on to Boston and enjoyed the *Lahey Clinic* for a week. I would recommend any surgeon to go a long way for the privilege of watching Dr. Frank Lahey remove a thyroid.

CARCINOID TUMOURS OF THE APPENDIX

By CHARLES NICHOLAS, F.R.C.S.

Assistant Director, Department of Surgery, Guy's Hospital.

EARLY case records described tumours associated with obliterative appendicitis which did not infiltrate widely or give rise to metastases, but which were nevertheless regarded as carcinomas until 1907, when Oberndorfer drew attention to their special characteristics and gave them the name of "carcinoids". He described the distinguishing features which characterize them to this day:—(1) Their localized nature and apparent benignity; (2) their slow rate of growth; (3) that more than one primary tumour may be present; (4) their characteristic microscopic appearance; (5) the absence of distant spread by lymph or blood stream.

CLINICAL FEATURES

Carcinoid tumours are said to be as frequent as 1 in 250 cases of appendicular disease, but this seems a high figure for a disease which a surgeon sees only a few times in his life. Twenty-five to thirty-five years is the most common age, and pain in the right iliac fossa is present in all cases. Some present as cases of recurrent appendicitis. According to Moore (1938), 60 per cent. of carcinoids are operated on as cases of acute obstructive appendicitis. A sausage-shaped swelling like an appendix wrapped round with omentum may be felt in the right iliac fossa. The following is an illustrative case:—

A patient, aged thirty-seven, was admitted to Guy's Hospital under the care of Sir Heneage Ogilvie, complaining of attacks of abdominal pain and vomiting. The pain was severe and continuous, first centered at the umbilicus, but later moving to the right iliac fossa. Vomiting occurred early in the attack. He had to go to bed for two days and then recovered completely.

On examination there was guarding in the right iliac fossa and a small, tender, fusiform, fixed swelling could be felt on the posterior abdominal wall lying parallel to, and two inches above, the right inguinal ligament.

Appendectomy was performed through a McBurney's incision. The appendix was lying over the pelvic brim, where it was firmly fixed by granulation tissue from which it had to be dissected, and numerous muco-fibrinous yellow granules escaped during separation. The appendix was generally thickened, the size of a finger, dull red in colour, and presented two swellings of cartilaginous consistency, like large cherries, involving its whole circumference, one at the tip and the other near the base. The appendix distal to the proximal swelling, which had completely occluded the lumen, was found to be a bag of pus. No enlargement of the regional lymph nodes was detected. The abdomen was closed in layers without drainage and the patient made an uneventful recovery. Microscopic examination revealed carcinoid cells, which had infiltrated the whole thickness of the appendicular wall with ulceration of the mucosa and dense subperitoneal fibrosis over the tumours. Although carcinoid tumour was suspected at operation, the diagnosis remained uncertain until the microscopic report was received; but even had the diagnosis been made, a more radical operation would not have been indicated in view of the lack of evidence of malignancy in previously recorded cases.

At operation, obstructive appendicitis may be found to be caused by a firm, rubbery, golden-coloured tumour about the size and shape of a cherry. The tumour may be anywhere in the wall of the appendix and, although

the tip is a common place, only those near the base can cause obstructive appendicitis. Tumours are usually single but may be multiple, as in the case described; they may be annular or involve only part of the wall. The peritoneum and immediate surroundings of the appendix may be inflamed and adherent. In the case described the appendix was firmly adherent over the pelvic brim and golden mucilaginous bodies escaped during the course of dissection. In but few cases does the disease spread to the regional lymph nodes, and in late cases which have not been submitted to operation the disease may infiltrate the cæcum and tissues of the right iliac fossa. In only one case (Callender, quoted by Shaw, 1925) have metastases been found at any far distant point; in this case in the liver.

The tumours consist of masses of spherical cells, some of which are arranged as rosettes lying in a fibro-muscular stroma which is condensed to form a capsule at the periphery. Some cells are spherical or polygonal with round distinct nuclei and cytoplasm containing lipoids, giving the golden colour so characteristic of the tumour; some contain granules which stain with chrome salts and give the argentophyl reaction; some are more rectangular and give an appearance of palisading, whilst others are columnar and form small rosettes.

Carcinoid tumours were formerly considered to be a variety of adenocarcinoma or basal-celled carcinoma, but the opinion of Gosset and Masson (1914) has now received general acceptance. They found that the Kultschitzky cells between the columnar cells of the crypts of Lieberkühn would take up ammoniacal silver salts in the same way as the cells of carcinoid tumours, formulated the theory of the origin of these tumours from these cells, and gave to them the name of "argentaffin tumours". They found these Kultschitzky cells present throughout the alimentary tract, but particularly plentiful in the appendix and terminal ileum. Although it is theoretically possible for carcinoids to develop anywhere in the alimentary tract, recorded cases are confined to the small bowel and appendix.

Treatment.—Nothing more than simple appendicectomy is usually called for, but if the diagnosis is made during operation and there is local infiltration and involvement of the regional lymph nodes, conservative removal of bowel and lymphatics should be carried out.

The malignancy is variously stated because of the inclusion in the data of cases of true adenocarcinoma of the appendix. When these cases were excluded Stewart and Taylor (1926) could find only eight examples of clinical malignancy in several hundreds of recorded cases, in spite of the invasion of the muscle layers which is a constant pathological finding.

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HYSTERECTOMY FOR NON-MALIGNANT CONDITIONS

By C. M. OTTLEY, B.M., F.R.C.S.

Surgeon, New Sussex Hospital for Women, and the Marie Curie Hospital.

OPINIONS differ as to whether, when abdominal hysterectomy is to be done for non-malignant disease of the uterus, the complete or the subtotal operation is preferable. To form a judgment it is necessary to consider the comparative risk of the two operations and the possible disadvantages of leaving the cervical part of the uterus behind. Study of two groups of consecutive operations, comprising respectively 300 subtotal and 300 total hysterectomies, carried out at the New Sussex Hospital by members of the surgical staff, shows that in each group two patients died, so that the mortality rate was 0.66 per cent. for each type of operation.

SUBTOTAL HYSTERECTOMY

It is fair, as Ahlquist (1942) points out, to add to the immediate post-operative mortality of the subtotal operation the mortality attached to subsequent carcinoma of the cervical stump and to procedures used in treating it. An early primary growth may be present although unrecognized at the time of operation. Many cases have been reported also of "cervical stump" primary carcinoma, arising after an interval long enough to justify the belief that the growth was not present at that time. Pearce (1934), who has followed up 810 cases of subtotal hysterectomy for at least five years, estimates the incidence of primary stump carcinoma at 1 per cent.; Meigs (1936), in a series of 1,774 cases, found an incidence of 0.73 per cent. Undiagnosed carcinoma of the cervical canal or corpus uteri may be present at the time of operation; as in the case (not included in the present series, which consists only of patients in whom the uterine condition was proved by subsequent microscopic examination to be non-malignant) of a spinster aged seventy-three years with an enormous fibroid uterus, which was removed by subtotal hysterectomy, and an early adenocarcinoma of the fundus. Recurrence may then take place in the cervical stump. Sarcomatous metaplasia of a fibromyoma is another possibility.

The cervix, being but a part of the uterus, is liable to share in any of the non-malignant conditions for which hysterectomy may be undertaken. It appears probable that when the uterus requires removal the cervix is seldom perfectly normal. In my last 100 cases of total hysterectomy for non-malignant conditions only two cervixes showed a normal histological structure; in the remaining 98 the pathologist's findings were:—

Inflammatory infiltration..	66	Congestion	9
Fibrosis	47	Mucous polypi	5
Atrophic mucosa	28	Dilated glands	3
Ovula Nabothii	10	Erosion	3

It is a fair assumption that at least some of these cervixes would have given trouble. Tyrone and Weed (1943) report a series of 44 patients in whom symptoms due to chronic cervicitis were present before subtotal hysterectomy and persisted after operation. Fibrotic changes, with atrophy of the mucosa, are often associated with fibrosis uteri, and may facilitate the occurrence of infection at a later date. Tuberculous endometritis may involve the cervix. Necrosis of one half of the cervical stump, due to interference with its blood supply, has been observed by Frank (1945). The stump may become the seat of a fibroid. The possibility that malignant disease may arise in the cervical stump has already been discussed.

TOTAL HYSTERECTOMY

The complete operation is somewhat more lengthy and more bloody than the subtotal and can be much more difficult, especially when large fibroids are present or when the patient is very fat. For these reasons subtotal hysterectomy may be preferred for a woman who is a poor surgical risk. In some cases of fibroids it is worth while to improve the access by removing some of the tumours before starting on the hysterectomy; a procedure which may also be of great assistance in dealing with severe bleeding in the course of the operation. It is important to keep the dissection quite close to the uterine wall and, by stopping all bleeding at once, to work in a dry field. These precautions minimize the danger of injury to the ureters or other neighbouring structures. In the present series no instance of such injury occurred among the total hysterectomies. One case of accidental division of a ureter occurred in the group of subtotal hysterectomies. By cutting through the vaginal wall at its junction with the cervix it is possible to avoid any shortening of the vagina and consequent interference with coitus. If it is thought desirable to anticipate the possibility of prolapse of the vaginal walls the round ligaments can be stitched to the cut edges of the vagina.

CONCLUSION

These two groups of cases, so far as they go, lend support to the view that the advantages which must be conceded to total hysterectomy are not outweighed by any additional risk as compared with the subtotal operation, at any rate when the patient is in reasonably fit condition. Subtotal hysterectomy will probably keep its place as the operation of choice when (as will rarely be the case) the paramount consideration is speed.

I am indebted to my colleagues on the staff of the New Sussex Hospital for permission to use the notes of their cases.

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CURRENT THERAPEUTICS

III.—BAL

By MILES WEATHERALL, B.M., B.Sc.

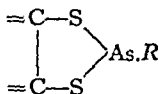
Lecturer in Pharmacology, Edinburgh University.

SINCE the beginning of the present century evidence has been accumulating that the proteins of living tissues contain $-SH$ or thiol groups, and that these groups are important for the normal functions of the tissues. In 1908, Ehrlich showed that arsenicals possessed a high affinity for $-SH$ groups, and it was suggested that the toxic action of various arsenicals was due to the combination of arsenic with tissue thiols and consequent blocking of their normal activities (Voegtlin *et al.*, 1923; Walker, 1928; Rosenthal, 1932).

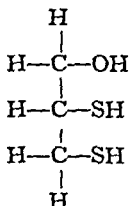
Voegtlin *et al.* (1923) showed that simple monothiols such as cysteine were effective prophylactics against arsenical poisoning both in mammals and in protozoa, and it was later found (Walker, 1928) that poisoned protozoa could be revived by thiol given after the arsenical. The observation of Cohen, King and Strangeways (1931) that compounds formed by combination of arsenic with thiol groups dissociated in alkaline solution gave grounds for believing that, if combination occurred between arsenic and thiols *in vivo*, the combination might be reversible.

These and other facts provided a starting-point in the researches for an antidote to the arsenical war gas, lewisite, initiated by Peters and his associates (1945) at Oxford at the beginning of the second world war.

In the course of this work Stocken and Thompson (1946), studying the most readily accessible thiol-rich protein, keratine, showed that it combined with lewisite when it was in the reduced ($-SH$) form but not when oxidized to the disulphide ($-S-S-$) form by linkage of two $-SH$ groups with the removal of hydrogen. The amount of arsenic taken up was closely related to the $-SH$ content of the protein, and it appeared likely that each atom of arsenic was combined with two adjacent $-SH$ groups, giving a stable ring configuration:—



It was likely that simple organic dithiols would form similar rings equally or more stable. This was found to be the case, and such compounds were tested for anti-arsenical activity on biological systems *in vitro* and *in vivo*. Among the earliest tried, for reasons of its lipid solubility and ability to penetrate skin, was 2,3-dimercaptopropanol:—



This substance formed a complex with lewisite much less dissociable than the lewisite-keratine complex. It protected and even reversed well-established poison-

It is a fair assumption that at least some of these cervixes would have given trouble. Tyrone and Weed (1943) report a series of 44 patients in whom symptoms due to chronic cervicitis were present before subtotal hysterectomy and persisted after operation. Fibrotic changes, with atrophy of the mucosa, are often associated with fibrosis uteri, and may facilitate the occurrence of infection at a later date. Tuberculous endometritis may involve the cervix. Necrosis of one half of the cervical stump, due to interference with its blood supply, has been observed by Frank (1945). The stump may become the seat of a fibroid. The possibility that malignant disease may arise in the cervical stump has already been discussed.

TOTAL HYSTERECTOMY

The complete operation is somewhat more lengthy and more bloody than the subtotal and can be much more difficult, especially when large fibroids are present or when the patient is very fat. For these reasons subtotal hysterectomy may be preferred for a woman who is a poor surgical risk. In some cases of fibroids it is worth while to improve the access by removing some of the tumours before starting on the hysterectomy; a procedure which may also be of great assistance in dealing with severe bleeding in the course of the operation. It is important to keep the dissection quite close to the uterine wall and, by stopping all bleeding at once, to work in a dry field. These precautions minimize the danger of injury to the ureters or other neighbouring structures. In the present series no instance of such injury occurred among the total hysterectomies. One case of accidental division of a ureter occurred in the group of subtotal hysterectomies. By cutting through the vaginal wall at its junction with the cervix it is possible to avoid any shortening of the vagina and consequent interference with coitus. If it is thought desirable to anticipate the possibility of prolapse of the vaginal walls the round ligaments can be stitched to the cut edges of the vagina.

CONCLUSION

These two groups of cases, so far as they go, lend support to the view that the advantages which must be conceded to total hysterectomy are not outweighed by any additional risk as compared with the subtotal operation, at any rate when the patient is in reasonably fit condition. Subtotal hysterectomy will probably keep its place as the operation of choice when (as will rarely be the case) the paramount consideration is speed.

I am indebted to my colleagues on the staff of the New Sussex Hospital for permission to use the notes of their cases.

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a characteristic unpleasant odour. It is moderately soluble in water and readily soluble in fat solvents. In solutions exposed to air, BAL decomposes fairly rapidly, especially if traces of metals are present, which catalyze oxidation. For clinical use BAL is put up in oily solutions containing benzyl benzoate, sterilized in nitrogen-filled ampoules, in which form BAL is stable for many months.

Toxicology.—The lethal dose of BAL for laboratory animals lies between 50 and 150 mgm./kgm. Death is preceded by peripheral circulatory failure and convulsions. In man, BAL by intramuscular injection does not produce any symptoms in doses less than 3 to 5 mgm./kgm. Single doses of up to 8 mgm./kgm. cause lachrymation, salivation, vomiting and a rise of blood pressure, but these effects disappear completely within a few hours, and subsequent damage is not known to occur. Abscesses at the site of intramuscular injection have been reported rather frequently, but mostly in cases of exfoliative dermatitis, when adequate cleaning of the skin obviously presents difficulties. Their significance is therefore difficult to assess.

Metabolism.—After intramuscular injection BAL is probably distributed fairly evenly throughout the body. It is concentrated in the kidney and excreted in the urine, probably largely in a combined form, in the first few hours after injection. The effects of a single dose largely disappear within four hours and, for maximum therapeutic effect, this appears to be the best interval between doses. BAL is comparatively ineffective by mouth.

Actions in experimental poisoning.—The experimental evidence indicates that in acute poisoning by various arsenicals, and probably in poisoning by other metals, BAL on the whole transfers the toxic element from the cells to the tissue fluids, particularly the plasma, and thence to the urine. In later stages of arsenical poisoning, when often only traces of arsenic remain in the body, effects of BAL in increasing excretion may be too small to be detected. It has nevertheless been shown that after treatment with BAL all instead of some of the arsenic held by lewisite poisoned skin is extractable by organic solvents (Graham, Levvy and Chance, 1947), and this change probably reflects greater mobility of the arsenic *in vivo*.

THERAPEUTIC USES

The experimental evidence suggests that the clinical applications of BAL may be widespread, and it is likely that all of its possibilities, as well as all of its hazards, have not yet been realized. Clinical experience with BAL so far reported deals with various arsenical intoxications occurring mostly during the treatment of syphilis, with acute mercury poisoning and with toxic reactions occurring during the therapeutic use of gold salts (table 1). BAL has been used mainly by intramuscular injection in the thigh or gluteal region, in courses similar to those described by Peters *et al.* (1947), that is:—

First day: four injections, each of 2 c.cm. of 5 per cent. BAL, at four-hourly intervals.

Second, third and fourth days: 2 c.cm. twice daily.

ing of enzyme systems and of animals by lewisite, and in all these respects was far more efficacious than any known monothiols.

This discovery was communicated to Americans and Canadians working on similar problems, and was confirmed by them (Waters and Stock, 1945; Young, 1946). The Americans gave to 2,3-dimercaptopropanol the name "British Anti-Lewisite" or "BAL", and widespread investigations were made into the biochemical, pharmacological and clinical properties of BAL and related substances. The ability to form complexes with thiols is not confined to arsenic, and the efficacy of dithiols has been tested in many other types of poisoning by heavy metals and metalloids. With certain exceptions, to be mentioned later, no dithiol has yet been found to supersede BAL, and the fact that it was almost the first dithiol to be selected for trial by Peters and his associates is noteworthy.

PHARMACOLOGICAL PROPERTIES OF BAL

The fundamental property of BAL is its ability to form stable complexes with arsenic and other metals. It is reasonable to expect it to be therapeutically useful in poisoning by any such element, although this depends upon the assumption that the complex so formed is less toxic than the parent element. This assumption is not necessarily true, but there is little evidence that the formation of complexes with enhanced toxicity is a practical danger. The possibility must be borne in mind whenever BAL is used in a metallic intoxication in which its efficacy is not established. As the action of BAL is on the toxic element rather than on injured tissues, it is not reasonable to expect it to be useful in lesions resembling, but not due to, metallic poisoning. It is not, for example, a general antivesicant although it is very effective in treating the blisters produced by lewisite. It must be remembered that BAL prevents therapeutic as well as toxic actions. It is as effective in protecting or curing arsenic-poisoned trypanosomes and spirochætes as in curing their hosts, and it abolishes the diuretic as well as the cardiac inhibitory actions of organic mercurials. The prophylactic use of BAL as a concomitant to the therapeutic use of these elements therefore defeats the purpose of the therapy and should not be practised. Against therapeutically used toxic elements BAL is indicated when, but not until, toxic manifestations appear. As the efficacy of BAL depends largely upon the formation of cyclic compounds, it is not likely to act appreciably against univalent elements; and it has no value in the treatment of argyria. Besides its activity against multivalent elements with an affinity for sulphur, BAL is a powerful reducing agent, and a carrier of -SH groups which may conceivably be of value in the economy of the organism. By virtue of the former property, BAL converts methæmoglobin to hæmoglobin, and has been shown to reduce experimentally produced methæmoglobinæmia in dogs, although it is less effective than methylene blue (Bodansky and Gutmann, 1947). This use perhaps merits clinical trial.

Physical properties.—Pure BAL is a colourless oil, denser than water, with

a characteristic unpleasant odour. It is moderately soluble in water and readily soluble in fat solvents. In solutions exposed to air, BAL decomposes fairly rapidly, especially if traces of metals are present, which catalyze oxidation. For clinical use BAL is put up in oily solutions containing benzyl benzoate, sterilized in nitrogen-filled ampoules, in which form BAL is stable for many months.

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Second, third and fourth days: 2 c.cm. twice daily.

Fifth and sixth days: 2 c.cm. daily.

However, in acute intoxications, up to nearly double these doses has been used "with considerable trepidation" but few ill-effects (Longcope and Luetscher, 1946). It should be noted that in all the trials considered here, treatment with BAL was supplemented by the relevant conventional therapeutic procedures, as should be the normal practice in its clinical employment.

Arsenical intoxications.—In cases of arsenical dermatitis occurring during antisymphilitic therapy, favourable results have occurred in 50 to 80 per cent. of the patients treated (Carleton *et al.*, 1946; Eagle and Magnuson, 1946; Peters *et al.*, 1947). As a rule, fever and skin œdema subside within a few days of giving BAL, and the patients rapidly feel better. Relapses sometimes occur but respond to a further course of BAL. The average time from

TABLE I
Therapeutic Uses of BAL

Conditions in which BAL is known to be effective:—

- Local and systemic poisoning by arsenical war gases
- Exfoliative dermatitis following arsenical therapy
- Arsenical encephalopathy
- Agranulocytosis following arsenical therapy
- Acute mercuric chloride poisoning
- Exfoliative dermatitis following gold therapy

Conditions in which BAL is known to be of doubtful value:—

- Aplastic anaemia following arsenical therapy
- Hepatitis following arsenical therapy

Conditions in which BAL is likely to be effective but in which its value has not been assessed clinically:—

- Toxic reactions to compounds of antimony, bismuth, gold and mercury (in addition to toxic reactions mentioned above)
- Methæmoglobinæmia from any cause

Conditions in which BAL may perhaps prove hazardous:—

- Poisoning by lead

Metallic intoxications in which BAL appears to be ineffective:—

- Argyria
- Poisoning by thallium compounds

administration of BAL to practically complete recovery is substantially less than usually observed without treatment. Treatment by inunction of ointments containing BAL is also effective, but painful; and it is interesting to note that Longcope *et al.* (1946), treating workers with dermatitis after exposure to diphenylamine chlorarsine dust, obtained as good results when the ointments were rubbed into areas of intact skin. BAL is absorbed readily by this route, and was therefore presumably acting systemically. There is probably no advantage, as a rule, in using inunction instead of injection. In other toxic reactions to arsenicals less data are available. Eagle and Magnuson (1946) report clinical improvement and a substantial reduction

in mortality in arsenical encephalitis when treatment with BAL was initiated less than six hours from the onset of cerebral symptoms. After six hours, BAL still appeared to be beneficial but its effects were less pronounced. In agranulocytosis or leucopenia after treatment with arsenicals, recovery is probably accelerated by BAL (Eagle and Magnuson, 1946; Holley, 1947), but insufficient cases have yet been reported to form a reliable conclusion. Results in aplastic anæmia are not encouraging, but quite inconclusive.

In post-arsenical hepatitis, BAL is not generally indicated, as results from its use have not been satisfactory (Eagle and Magnuson, 1946), and as the immediate cause of the hepatitis is probably often infective. Once liver infection is established, anti-arsenical treatment may be expected to be of little value, and in the presence of liver damage the toxicity of BAL may be enhanced (Cameron, Burgess and Trenwith, 1947). BAL has been used with good effect in patients who have accidentally received an overdose of mapharsen (Eagle and Magnuson, 1946).

Acute mercuric chloride poisoning.—Longcope and Luetscher (1946) report a mortality for acute mercuric chloride poisoning in patients admitted to Johns Hopkins Hospital of 34 out of 263 before 1945, and 2 out of 42 since the institution of treatment with BAL. When only patients who had swallowed 1 gm. or more of mercuric chloride and in whom treatment was started within four hours are considered, the mortalities become 27 out of 86 and 0 out of 25, respectively. There is little doubt that BAL is a highly effective form of treatment, provided that it is given as early as possible and with adequate supportive treatment.

Toxic reactions to gold salts.—A number of papers have appeared recently, all more or less optimistic, about the value of BAL in toxic reactions occurring during the treatment of rheumatoid arthritis with gold salts (Cohen *et al.*, 1947; Lockie *et al.*, 1947; Margolis and Caplan, 1947; Ragan and Boots, 1947; Slot and McDonald, 1947). In some, but not all, cases the dermatitis has subsided and there has been increased excretion of gold in the urine. Ragan and Boots mention also that the arthritis was exacerbated during treatment with BAL. This was not observed by Lockie *et al.*, who found improvement after BAL in one case of gold purpura and one of granulocytopenia.

CONTRAINDICATIONS AND DANGERS

Apart from the ill-effects of overdosage, the only untoward reaction to BAL reported in human subjects is the development of skin sensitization. Sulzberger *et al.* (1946) describe the occurrence of erythema, œdema and papules after the external application of BAL to the skin of previously exposed subjects. Sensitization occurred in about 20 per cent. of subjects in whom BAL had previously been applied to normal skin; in about 30 per cent. of those who had had repeated intramuscular injections, and in about 70 per cent. of those in whom BAL had been applied to damaged (chemically burnt) skin. The possibility of such reactions should not be overlooked, but

apparently they have not complicated the use of BAL in ordinary short-term courses or prevented the repetition of such courses when necessary.

Experimental observations in animals indicate several other possible risks in the use of BAL. What is probably the most important of these, enhanced toxicity in the presence of liver damage (Cameron *et al.*, 1947), has already been mentioned, and its application is obvious. Besides this, in certain experimental circumstances, BAL can enhance the toxicity of substances against which it is used. The compound formed by BAL and mapharside is more toxic than mapharside alone when administered intramuscularly in rats (Peters and Stocken, 1947), although complete protection is obtained by the use of excess BAL. This compound is also more toxic to various micro-organisms (Friedheim and Berman, 1947; Friedheim and Vogel, 1947), perhaps because its greater lipid solubility permits it to penetrate to intracellular sites not normally accessible to mapharside and there, for reasons not comprehended, to dissociate with the liberation of free arsenic. Koppanyi and Sperling (1947) have described an explosive reaction consisting of crying, motor excitement and parasympathetic overaction in rabbits given sodium arsenite intravenously shortly after BAL intramuscularly. The reaction was not produced by a mixture of BAL and arsenite prepared *in vitro* and, although alarming, was not fatal. Arsenates, arspenamines and mercury compounds did not elicit the reaction. With cadmium, BAL forms a complex which is considerably more toxic to the kidney than are free cadmium ions; and increased renal damage can be produced by BAL in cadmium chloride-poisoned rabbits (Gilman *et al.*, 1946). On the other hand, BAL prevents the nephro-toxic and renotrophic actions of lead in rats (Chiodi and Sammartino, 1947), diminishes the anæmia but apparently increases the porphyrinuria after a single large dose of lead acetate in rabbits (Weatherall, 1948), and increases the mortality in subacutely lead-poisoned rabbits (Braun *et al.*, 1946). Evidence of this sort indicates that the action of BAL does not consist entirely of the formation of innocuous and readily excreted metallic complexes, and is a warning against its casual use in any kind of metallic intoxication in which it might at first sight seem to be indicated.

It should also be mentioned that prolonged administration of fairly large doses of BAL to cats causes anæmia, loss of weight and a rise in blood non-protein nitrogen (Modell *et al.*, 1946). McCance and Widdowson (1946) have shown a substantial rise in the urinary excretion of copper and zinc in man after intravenous injection of "BAL-Intrav", the glucoside of BAL. The possibility exists that BAL has a similar effect which, if maintained, would remove these important trace elements from the body to a dangerous extent. There is no evidence that this can happen, but prolonged administration of BAL is not as a rule desirable. If no satisfactory response occurs to an ordinary course of treatment, there is no justification for continuing the use of BAL without, at least, allowing an interval for recuperation.

FUTURE POSSIBILITIES

Although no dithiol more generally satisfactory than BAL is yet known, new developments are not impossible. Particularly BAL glucoside or BAL-Intrav, a water-soluble derivative developed by Danielli and his associates (1947) at Cambridge, is promising because of its extremely low toxicity and good anti-arsenical activity. No clinical trials of this substance have been reported. Whilst the five-membered ring formed by BAL and arsenic is satisfactory from a therapeutic point of view, Barron *et al.* (1947) have shown *in vitro* that for other metals, other dithiols with a different spatial arrangement of -SH groups are more effective antidotes, and this observation may lead to new therapeutic agents for metallic poisoning in which BAL is not effective, or in which it is only slightly beneficial.

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REVISION CORNER

FLAT FEET

DURING the past war many Service men and women reported to the orthopaedic departments with symptoms of flat feet. Often it was not their first visit, as they had previously undergone many forms of treatment, including prolonged rest, exercises, physiotherapy of every type, manipulations with and without anaesthesia, and even plasters, without alleviation of their symptoms. The reason for this was that they were never instructed in the correct way to stand and walk. The patient must have a clear idea that he is carrying out exercises and treatment to strengthen certain muscles to withstand postural strain and allow him to throw the body weight on to those parts of the foot designed to bear them.

ETIOLOGICAL FACTORS

On studying the kinetographic prints of the normal foot, it will be observed that in standing the weight is carried on the heel, the outer side of the foot and the forefoot.

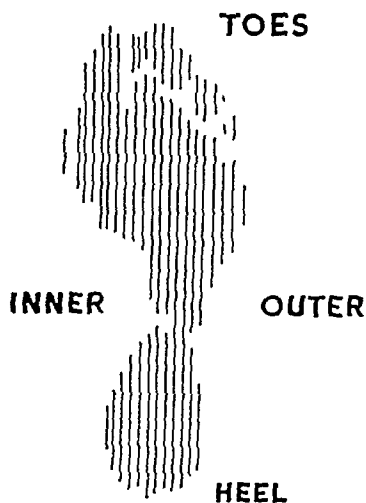


FIG. 1.—Kinetographic imprint of normal foot.

Wood Jones (1944) describes two distinct functions of the foot, the outer stabilized and static supporting part, and the inner part, considered the elastic dynamic organ which takes part in active propulsion. Lambrinudi (1942) stated that the outer part lies flat on the ground, gives the bigger weight-bearing surface and stability and balance with the aid of the fourth and fifth toes. It is essentially a balancing organ, whereas the inner portion is essentially a lever. For a comprehensive understanding of painful symptoms related to the feet it is essential to be aware of these two separate functions. As Mercer (1943) states, the functions of the feet are (a) the action of standing in which the postural muscles are in a static state, so that the weight is evenly distributed throughout. This is the passive action of the foot. (b) The action of walking or propulsion in which the foot muscles are moved actively, so that the heel-toe rhythm of walking is carried out.

The foot can therefore be said to contain

the following arches:—

(A) *The longitudinal arch* divided into two, the outer consisting of the os calcis, the cuboid and the fourth and fifth metatarsals, and the inner consisting of the talus, scaphoid, cuneiforms and three inner metatarsals. It is in this latter part of the foot that the concave longitudinal arch is seen, and its structure depends upon (1) the shape of the bones; (2) the integrity of the intertarsal ligaments, spring ligament and the long and short plantar ligaments and plantar fascia; (3) the tone of the long and short muscles of the foot, especially tibialis posticus and peroneus longus. Even in the embryo and in infancy this inner arch is well formed, but may not be so obvious as there is a greater preponderance of the soft tissues at this age.

(B) *The transverse arch* is seen from the kinetographic imprint to extend from the lateral border of one foot to the lateral border of the other. Wood Jones (1944), quoting Ellis, states that each foot is complimentary in constituting a plinth that bears the body weight and that the feet must not be regarded as two plinths, but as two halves of one divided.

(C) *The anterior metatarsal arch* is an imaginary concave arch extending from the first metatarsal head on the inner side to the fifth head on the outer side. In standing this arch is obliterated. Its strength depends upon the tone of the intrinsic muscles of the foot, and the intertransverse ligament between the metatarsal heads.

Morton (1935) associates a weak first metatarsal segment with painful conditions of the inner longitudinal arch, because it is the forward strut of this. There may be hypermobility of this segment, so that the first metatarsal is not taking its full share of weight bearing. There may also be associated shortening of the first metatarsal bone and the sesamoid bones may be placed posteriorly, so that the first metatarsal segment is unstable. Unless the muscles acting on the arches are in good postural tone, the inner longitudinal arch collapses, allowing the talus to progress forwards on to the spring ligament and with the sustentaculum tali and the tuberosity of the scaphoid become prominent on the inner side of the foot. It will be seen therefore that well-functioning feet depend almost entirely upon satisfactory postural tone of the controlling muscles.

Wood Jones (1944) has pointed out that it is wrong to compare the hand and the foot, because in the hand the flexor and extensor muscles are working as antagonists, whereas in the foot they are working in a complimentary fashion and really cannot be described as having origins and insertions. With the foot fixed on the ground the insertion becomes the *origin* and *vice versa*.

Lake (1935) suggests the classification of flat foot into :—(1) Congenital; (2) infantile; (3) adolescent, as faulty posture and spasmodic or spastic; (4) infective; (5) adult. This classification coincides in general with that of Mercer, who describes:—(1) Congenital flat foot; (2) acquired flat foot, which may be due to (a) osseous changes, (b) ligamentous changes, (c) muscular changes, either paralytic or spastic, and postural or static flat foot.

POSTURAL OR STATIC FLAT FOOT

Postural or static flat foot is by far the most common and will now be considered. As the effect of strain becomes more evident and pressure is brought to bear upon the intertarsal and the spring ligaments, and eventually upon the bones, so five different stages in flattening of the arch can be distinguished. It is naturally a gradual process and one stage merges into another. Mercer describes these stages as:—

- (1) The mild type of foot strain or incipient flat foot.
- (2) The voluntary flat foot. The arch has dropped, but secondary changes have not occurred.
- (3) The resistant flat foot. Secondary changes are beginning to occur.
- (4) The rigid flat foot. Osteoarthritis has supervened and it is impossible to correct the deformity unless the foot is forcibly wrenched under anæsthesia.
- (5) Permanent flat foot. Structural changes of such a marked degree have occurred that it is impossible to restore the arch even under anæsthesia.

Symptoms complained of when flattening of the arch occurs will be aching, pain, tenderness, swelling of the feet, walking splay foot, deformities appearing, stiffness, muscular spasm and callosities. As a result of foot strain and faulty gait extra strain may be thrown on the muscles of the knee and buttock and pain and aching may be experienced in these regions and even in the lower back. Varicose veins may develop.

Treatment.—Mercer points out that the object of treatment must be (1) the correction of the abnormal centre of gravity of the foot, so that the body weight is transferred to the outer side of the foot; (2) to remove pressure symptoms.

These can be accomplished by (a) massage; (b) contrast baths; (c) faradic stimulation of the small muscles of the foot and those of the calf and leg; (d) correction of foot wear; (e) remedial exercises, and (f) rest from excessive strain or walking.

If foot supports are given it should be understood that they may be of a temporary nature only. They can be of the following types, according to the severity of the flat foot and how much support is necessary:—(1) Leather and felt supports; (2) a

sponge rubber support; (3) the more rigid type made from duraluminium. They should be made from plaster casts and should fit perfectly.

When the foot has become stiff and rigid, a period of rest may be essential combined with bed exercises and contrast baths, but later, manipulation under full anæsthesia may become necessary in order to break down adhesions that have formed from tissue œdema. After the manipulation the patient must be given graduated exercises and further physiotherapy.

Operative treatment on the bones is confined to the rigid fixed foot and should not be carried out until all other methods fail.

FLAT FEET IN EARLY CHILDHOOD

These are often associated with genu valgum of varying degrees and treatment must be directed to this as well as to the feet. Usually inner wedges $\frac{1}{8}$ " to the heel and tread of the shoe, combined with inversion exercises and gentle manipulative cupping of the feet, remove strain and allow hypotonic muscles to strengthen, so that a well-formed arch is maintained.

The spasmodic or spastic flat foot in adolescence has been considered to be due primarily to spasm of the perineal muscles. Tonsillar infection has often been found to be present and should be eliminated. The children are often over-weight.

Lapidus (1946) has placed the lesion in the subastragaloid joint, especially involving the common interosseous ligament. He has described three degrees:—(1) The mild type, in which the patient can often be cured by a period of rest and exercise followed by the wearing of supports, closely fitting and of a rigid type. (2) The moderately severe type. Even this type responds to more prolonged rest, exercises and support. (3) The rigid fixed type in which operation on the subastragaloid and mid-tarsal joint may be necessary.

THE ANTERIOR TRANSVERSE ARCH

Treatment of painful conditions of this arch consists of tarsal pads and strengthening of the intrinsic muscles of the foot by contrast baths, massage, exercises, faradic stimulation and manipulation.

Morton's metatarsalgia has recently been described as due to a fibrous thickening or actual neuroma formation on the interdigital nerves, especially the third. If pain is severe and persistent, in spite of physical treatment and pads, operative removal of these thickenings is indicated. It must be remembered that Morton (1935) described an arthritis of the tarsometatarsal joints, especially the second, as one of the causes of the disease. The thickening caused by this arthritis involved the lateral branch of the plantar nerve, so that in treating these cases the tarsometatarsal joints must be included.

W. E. TUCKER, M.B.E., M.B., B.Ch., F.R.C.S.

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DIAGNOSIS AND TREATMENT OF SALPINGITIS

THE primary causes of salpingitis are:—(1) gonorrhœa (40 per cent. of cases); (2) infection following abortion or delivery (50 per cent.); (3) tuberculosis (5 per cent.); (4) infection from adjacent organs such as the appendix (5 per cent.).

ACUTE GONOCOCCAL SALPINGITIS

Gonococcal salpingitis is less common since the introduction of penicillin for the treatment of gonorrhœa. Upward spread to the tubes occurs after a short interval,

usually at the time of the succeeding menstrual period, and the risk of spread is increased by local instrumentation. Acute bilateral lower abdominal pain occurs, often associated with an excessive or aphasic menstrual period. There is fever of 102° to 103° F. (38.9° to 39.4° C.), which is higher than in most cases of appendicitis and a cardinal point in differentiation from a case of ectopic gestation. Vomiting is rare, nor are the oral fœtor and furred tongue of acute appendicitis present. Yellow vaginal discharge is usual, and there may be frequency. The lower abdomen is slightly distended, tender and guarded. On pelvic examination, cervicitis and urethritis may be found. Movement of the cervix or pressure in the fornices causes pain, and tenderness is usually so marked that the adnexæ cannot be defined, although after forty-eight hours ill-defined masses may be made out, consisting of the tubes matted to adjacent structures. A well-defined mass is *not* felt unless a pelvic abscess or a pyosalpinx forms, which takes some days; a point that excludes the diagnosis of a twisted ovarian cyst. Cervical and urethral smears and cultures may reveal gonococci.

Treatment of the primary attack is conservative, consisting of absolute rest, with a large fluid intake, and the injection of 20,000 units of penicillin three-hourly, to a total of about 300,000 units. All local interference is strictly avoided. Nearly all primary cases respond, although a few develop a pelvic abscess, when the temperature "swings", and a pelvic mass first enlarges and then softens; it is then drained by posterior colpotomy. Pyosalpinx is a rare sequel of a single attack, but if the temperature does not settle after fourteen days, salpingostomy has been recommended, in the hope that early incision and drainage of a pus tube will prevent complete destruction; the hope seems slender. On the other hand it is reasonable to test tubal patency three months after resolution of a first attack as there is more hope of successful salpingostomy then than later. Lipiodol salpingography at this time is not without risk, and should never be performed unless the erythrocyte sedimentation rate is normal, and there are no signs of residual tubal or cervical infection.

SALPINGITIS FOLLOWING DELIVERY OR ABORTION

In these cases the history is entirely different; salpingitis is part of widespread pelvic cellulitis and peritonitis, and is often only revealed after three or more weeks when the widespread infection recedes. The diagnosis is seldom in doubt: after several days of fever following delivery or abortion there is a further rise of temperature, with lower abdominal pain, distension or guarding, and bilateral tubal masses ultimately become palpable. Most puerperal cases are due to streptococci which are sensitive to penicillin, and the initial treatment is the same as for gonococcal salpingitis, although more care is needed to treat anæmia and sustain the general resistance, and surgery will be necessary if resolution does not occur.

RECURRENT AND CHRONIC SALPINGITIS (OTHER THAN TUBERCULOUS)

Recurrent subacute attacks.—Gonococci and streptococci do not survive indefinitely in the tube; the contents of a pyosalpinx are nearly always sterile. Recurrent attacks of salpingitis are usually due to reinfection, often by a secondary invader such as *B. coli*, but sometimes from a persisting focus in the lower genital tract, or by reinfection by a consort. In such an attack there is pain and fever, and tubo-ovarian masses are found behind the uterus, which may become fixed in retroversion. The tubal swellings are nearly always bilateral, although of unequal size. Irregular and excessive menstruation often occurs, due to abnormal production of œstrogens by the ovaries, which contain multiple follicular cysts.

"Burnt-out" salpingitis.—Even in cases in which no active infection persists there may still be severe symptoms. There may be pain due to pelvic adhesions, sometimes with backache or dyspareunia. Menorrhagia or sterility may be the primary complaint. Except in the case of a hydrosalpinx there is no large tubal mass, although

sponge rubber support; (3) the more rigid type made from duraluminium. They should be made from plaster casts and should fit perfectly.

When the foot has become stiff and rigid, a period of rest may be essential combined with bed exercises and contrast baths, but later, manipulation under full anæsthesia may become necessary in order to break down adhesions that have formed from tissue œdema. After the manipulation the patient must be given graduated exercises and further physiotherapy.

Operative treatment on the bones is confined to the rigid fixed foot and should not be carried out until all other methods fail.

FLAT FEET IN EARLY CHILDHOOD

These are often associated with genu valgum of varying degrees and treatment must be directed to this as well as to the feet. Usually inner wedges $\frac{1}{4}$ " to the heel and tread of the shoe, combined with inversion exercises and gentle manipulative cupping of the feet, remove strain and allow hypotonic muscles to strengthen, so that a well-formed arch is maintained.

The spasmodic or spastic flat foot in adolescence has been considered to be due primarily to spasm of the perineal muscles. Tonsillar infection has often been found to be present and should be eliminated. The children are often over-weight.

Lapidus (1946) has placed the lesion in the subastragaloid joint, especially involving the common interosseous ligament. He has described three degrees:—(1) The mild type, in which the patient can often be cured by a period of rest and exercise followed by the wearing of supports, closely fitting and of a rigid type. (2) The moderately severe type. Even this type responds to more prolonged rest, exercises and support. (3) The rigid fixed type in which operation on the subastragaloid and mid-tarsal joint may be necessary.

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ACUTE GONOCOCCAL SALPINGITIS

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tuberculous peritonitis, although simple drainage of ascitic fluid seems beneficial. If the disease is strictly localized to the pelvic organs bilateral salpingo-oophorectomy gives excellent results, and this treatment is often applied to cases discovered by laparotomy. X-ray therapy has many advocates, but the results seem to be less certain than with surgery.

S. G. CLAYTON, M.D., M.S., F.R.C.S., M.R.C.O.G.

NOTES AND QUERIES

Temperature Charting in Relation to "The Safe Period"

QUERY (from Portugal).—I have read recently some articles on the alteration in the body temperature at different times in the menstrual cycle, being lower in the follicular phase and higher during the luteal phase, and the use of these findings, by the temperature chart taken daily on waking, as a method of avoiding the time when pregnancy is most likely to occur in those who do not wish to use contraceptives. I have not yet seen anything written about the practical way to apply the method.

REPLY.—The fact that fluctuations in the basal body temperature take place in women during different phases of the menstrual cycle was noted by van der Velde as long ago as 1904. These fluctuations have in recent years been correlated with the various events that take place during the cycle. The changes can be briefly summed up as follows:—

From the beginning of menstruation until the time of ovulation the temperature is at a comparatively low level, and fluctuates by about five-eighths of a degree Fahrenheit. At the time of ovulation there is a drop of basal body temperature of one half a degree or more, followed the next day by a rise of over one half of a degree. During the second half of the cycle, normally the period of activity of the corpus luteum, the temperature remains at the higher level until a day or two before the onset of the next menstrual period. If pregnancy occurs, there is no drop but a continued rise.

This biphasic curve of basal body temperature is characteristic of the normal ovulatory menstrual cycle, and in cases in which the cycle is anovulatory the rise in the second half of the cycle is absent. The occurrence of regular menstrual cycles in association with a biphasic curve of basal body temperature permits of accurate estimation of the time of ovulation. The temperature must be taken under basal conditions. The woman is instructed to keep a thermometer by her bedside and to take her temperature immediately on waking in the morning. The temperature may be taken by mouth or per rectum and should be immediately recorded.

The method has many practical applications. It may be used as a precise means of calculating the "safe period", that is, the time during the menstrual cycle when conception is unlikely to occur. The assumption is made that spermatozoa are capable of fertilizing an ovum for

about forty-eight hours and that the period of viability of the ovum is about the same length of time. The infertile, or "safe", period can be assumed to begin five days after ovulation. The original method of determining the "safe period" according to the method of Ogino and Knaus was based on the average length of the menstrual cycle. It was assumed that conception was unlikely to occur in the week preceding menstruation. Failure of the Ogino-Knaus method might occur from a late ovulation, but this would presumably be detected by the method of recording of temperatures. Another possible cause of failure is the occurrence of more than one ovulation during a single menstrual cycle. This second ovulation would presumably not be detected by the temperature chart, but it may also presumably be regarded as an uncommon event and thus as an unlikely source of error.

JOSEPHINE BARNES, D.M., F.R.C.S., M.R.C.O.G.

Status Epilepticus

QUERY.—I shall be grateful for some information on status epilepticus. I have an interesting case of a middle-aged woman, who had an attack of status epilepticus six months after artificial menopause. She has suffered from epilepsy for twenty odd years, and is married with two children. She has only had this one attack. Could you tell me if she is likely to have another and, if so, how to prevent it?

REPLY.—Status epilepticus is simply a descriptive term used when epileptiform attacks, whatever be their cause, recur rapidly without consciousness being regained between them. It may last for hours or even days and, unless suitable treatment is instituted, frequently proves fatal. There is often an accompanying hyperthermia. A common cause of status epilepticus in long-standing epilepsy is the sudden withdrawal of an anticonvulsant drug, such as phenobarbitone, which has been taken for long periods. Gradual weaning of these drugs is essential. The best preventive of status epilepticus is adequate and continuous control of the sporadic fits, but should it occur the patient should be given 3 to 5 grains (0.2 to 0.32 gm.) of soluble phenobarbitone by intramuscular in-

the uterus is often fixed in retroversion, and there may be induration in the fornices due to fibrosis. Especially after abortion, tubal damage may occur insidiously and only be discovered during subsequent investigation of sterility.

The *diagnosis* of chronic salpingitis can be difficult. Endometriosis gives a similar clinical picture, with pain, sterility, menorrhagia and pelvic masses, although there is no history or evidence of infection. A specialist sees many women with menorrhagia or retroversion, in whom underlying salpingitis has been overlooked. On the other hand, salpingitis is too freely diagnosed in cases without history of infection or previous pregnancy, and without abnormal pelvic physical signs.

The indications for *surgical treatment* of chronic salpingitis cannot be rigidly defined. Obviously every effort is made to conserve or restore function in a young nullipara, but once function is irretrievably lost radical treatment is preferable to prolonged ill health or repeated episodes of painful incapacity. Conservative treatment consists of rest, penicillin in exacerbations, and local heat. Pelvic diathermy must be used cautiously as it sometimes lights up latent infection. Indications for surgery may be summarized thus:—

- (1) For cases with recurrent attacks, or when conservative treatment fails to relieve pain
- (2) For cases with large masses, as they seldom respond to conservative treatment, and because the diagnosis may be in doubt.
- (3) For cases with menorrhagia.
- (4) For selected cases of sterility

Patients are in two categories; those with hopelessly damaged tubes, and the minority in whom tubal recovery is possible. In the former, radical excision of infected structures is required, but with conservation of some ovarian tissue wherever possible. If bilateral salpingectomy is necessary then total hysterectomy is often wise, as the cervix is infected and menorrhagia may also be a sequel. Widespread adhesions can make this a difficult operation, but a clean sweep is preferable to piecemeal assault.

In a few cases of sterility attempts may be made to restore tubal patency. If there are no clinical signs of activity and the E.S.R. is normal, a lipiodol salpingogram will demonstrate the site of occlusion. If only the abdominal ostium is closed there is a 10 per cent chance of success by salpingostomy. In other cases with blockage at the uterine cornu the tube can be reimplanted into the uterus, but the state of the outer part of the tube can only be determined by laparotomy, when it is usually found to be hopelessly damaged, so that the percentage of cases in which success follows laparotomy is much lower than 10 per cent. Scrupulous technique is essential, with perfect hemostasis and accurate stitching with bland suture material. "Amnioplastin" has been used to cover suture lines (with doubtful benefit), and a nylon strand may be laid along the tubal lumen, with the lower end passing through the uterus, so that it can be withdrawn from below after a few days. Oestrogens will assist nutrition and regeneration of the tube.

TUBERCULOUS SALPINGITIS

A confident clinical diagnosis is made in only a proportion of cases. If a nullipara without history or evidence of cervicitis has salpingitis, tuberculosis should be considered; especially if the disease is of insidious onset with loss of weight and slight pyrexia, although superimposed acute attacks may be due to secondary infection. Menorrhagia is common, but amenorrhœa occurs in advanced cases. Tuberculous ascites or plastic peritonitis may be found, or pyosalpinges felt. In 20 per cent. of cases there is active pulmonary disease.

In many cases the *diagnosis* is only made at operation for chronic salpingitis, when tubercles are seen on the tubes or pelvic peritoneum; or at curetting for menorrhagia when tuberculous endometritis is discovered. Sharman found tuberculous endometritis in 5 per cent. of cases of sterility due to tubal occlusion, without other evidence of tuberculosis.

Opinions differ about *treatment*. If there is active pulmonary disease sanatorium treatment is advised; and radical surgery is most unwise if there is widespread

PRACTICAL NOTES

Vitamin E Deficiency and Vascular Disease

THAT deficiency of vitamin E may play a part in the genesis of vascular disease is indicated by the results obtained by E. V. Shute, A. B. Vogelsang, F. R. Skelton and W. E. Shute (*Surgery, Gynecology and Obstetrics*, January 1948, 86, 1), who have treated a series of cases of vascular disease, including thrombophlebitis, indolent ulcers of the legs, gangrene of the extremities, and thromboangiitis obliterans, with *a*-tocopherol. The dosage employed was from 200 to 300 mgm. daily, by mouth, except in acute cerebral thrombosis, when the drug should be given parenterally in order to procure early saturation of the patient to minimize the risk of brain cell damage. It is stressed that the vitamin E employed must be *a*-tocopherol, and no inorganic iron should be administered to the patients. In three cases of thrombophlebitis, one ante-partum and one post-partum, 200 to 300 mgm. of *a*-tocopherol daily by mouth resulted in clearing of the condition in an average of four weeks. In a case of ulceration of the leg of nineteen years' duration, in a sixty-three year old man, 250 mgm. of *a*-tocopherol daily by mouth resulted in complete healing in ten weeks. A case of dry gangrene of the feet and legs, in a man of seventy-four, responded well to 300 mgm. of *a*-tocopherol daily by mouth, and just over one month later both feet were healed and the patient began to walk. On admission this case was regarded as one for amputation of both legs. Two cases of thromboangiitis obliterans are also recorded, in both of which good results were obtained. It is stated that although the group studied was small the results of the therapy were encouraging, and may indicate a valuable addition to the prophylaxis of vascular diseases. It is necessary to continue the *a*-tocopherol at a high level after healing has been obtained, as in some cases relapse occurred when treatment was stopped.

The Treatment of Furunculosis

ALTHOUGH usually benign, boils may be dangerous on account of their recurrent nature, and even the most innocent boil may prove to be the portal of entry of a serious staphylococcal infection. These facts are stressed by Y. Pécher (*Presse Médicale*, Suppl., January 7, 1948, 56). In diabetics boils are of common occurrence, but even in non-diabetics carbohydrates should be restricted in the presence of boils, and particularly bread and sugar. Special attention is drawn to the danger of boils on the upper lip and nose. If not interfered with and so

aggravated they may evolve as ordinary boils, but rapid abortion can be procured by one or two applications of X-rays in low dosage. General treatment consists of thiazamide, 8 gm. daily, and 20 drops of Lugol's solution three times daily for six days; or better, penicillin in dosage of 600,000 units. Penicillin is also advocated for the treatment of furunculosis, 300,000 units daily for three days; and when boils become infected, and particularly when on the face, intensive penicillin therapy should be carried out with a dose of 1,000,000 units on the first day, treatment being continued for as long as necessary.

Aerosporin in the Treatment of Whooping-Cough

AEROSPORIN is an antibiotic produced by an aerobic spore-bearing bacillus, *Bacillus aerosporus* or *B. polymyxa* which has been isolated from soil and air. Tests have shown it to be active against gram-negative organisms, and in experimental infections in animals it gave complete protection against *H. pertussis* and elimination of the infection. A report of the clinical use of aerosporin in ten cases of whooping-cough is given by P. N. Swift (*Lancet*, January 24, 1948, i, 133). The patients treated were children of ages ranging from 1 month to 2½ years, and the dosage employed was 0.4 mgm., by intramuscular route four-hourly, in mild cases, and 0.8 mgm. four-hourly or three-hourly in severe cases, treatment being continued for five days. There was a definite response in all cases, mostly within the first forty-eight hours; vomiting, apnoea, cyanosis and frequency of paroxysms first diminishing and, finally, the whooping and cough. Two cases proved fatal, but in both treatment with aerosporin was not started until secondary invasion had occurred. The best results were obtained in those cases in which treatment was begun early in the illness before secondary infection, and in such cases aerosporin alone proved effective: in four cases penicillin was given in conjunction, and in two of these cases sulphadiazine as well. A form of transient albuminuria occurred in most of the patients, but disappeared within a week; it was considered to be associated with impurities in the preparation used. This is a preliminary report of some interest, although aerosporin is not yet generally available.

Procaine Penicillin G (Duracillin)

THE results of preliminary clinical trials with procaine penicillin G (duracillin: Eli Lilly & Co.) are recorded by W. E. Herrell, D. R.

jection, and 1 to 2 grains (0.065 to 0.13 gm.) should be repeated at four-hourly intervals until consciousness is regained, when 1 grain (65 mgm.) of phenobarbitone should be given by mouth four-hourly, and the dose gradually reduced. Other measures have been advocated:—paraldehyde per rectum, basal anæsthetics such as pentothal, chloroform anæsthesia, and curarization; but the method here described is simple and effective. When an oxygen tent is available, the patient benefits from being treated in it. Provided the patient is adequately treated the attacks should be satisfactorily controlled, and the likelihood of status epilepticus rendered extremely remote, but sudden cessation of anti-epileptic treatment will almost certainly precipitate a recurrence.

HENRY COHEN, M.D., F.R.C.P.

Giant Urticaria in an Infant

QUERY.—I have a little girl patient, aged one year five months, who for the past nine months has had recurring attacks of urticaria, the skin being quite clear between attacks. The rash invariably affects the lower abdomen, and the back just above the napkin area. It is a typical giant urticaria. When it first appeared it affected body, limbs, and face in turn. I have failed to find any allergic food. The mother suffers from asthma, and a brother of the child's father also suffered from asthma. The child is otherwise normal and healthy. Benadryl elixir gave a decided improvement earlier on but is now without effect, as is ephedrine. Local applications, such as lead and calamine lotion, zinc and eucalyptol ointment, gave only passing relief. The child wakes twice or three times nightly and cries lustily; in daytime she is quite happy. Can you suggest any further treatment? What sedative (orally) would you suggest at night? Would you say the family history leaves the child predisposed to this allergic reaction? Should antihistamine be worth a trial? The attacks are sometimes associated with teething.

REPLY.—Giant urticaria is rather rare in young children. Certainly the family history indicates some hereditary predisposition. Its present localization and its intermittent character suggest the possibility of a local factor such as a tight-fitting garment, perhaps one that is sometimes worn at night. Other physical causes may be responsible, e.g., hot baths. Although not entirely reliable, routine scratch tests may indicate a specific allergen, especially if this is an inhalant. With regard to the alimentary tract, if foods have been definitely exculpated (it is unlikely from the history to be a daily food) the stools should be examined for worms

and for evidence of bacterial putrefaction. In the latter case mercury with chalk may prove curative. Other sources of infection or intoxication, such as septic tonsils, should be looked for. Finally, some cases of urticaria are produced by excitement. As a symptomatic remedy antihistamine (M & B) or antistin (Ciba) may prove more helpful than benadryl. As a night sedative I suggest:—

R		
	Ammonium bromide ..	1 grain (65 mgm.)
	Tincture of belladonna	2 minims (0.12 c.cm.)
	Chloroform water	to 60 minims (3.6 c.cm.)
or:		
R		
	Potassium bromide	2 grains (0.13 gm.)
	Chloral hydrate	3 grains (0.2 gm.)
	Syrup of oranges	10 minims (0.5 c.cm.)
	Chloroform water	to 60 minims (3.6 c.cm.)

W. N. GOLDSMITH, M.D., F.R.C.P.

Hypertension with Normal Renal Function

QUERY (from Iraq).—I have a patient, a man aged forty-five, who came to see me a year ago for some gastric trouble. On examining him I was astonished to find that he had a very high blood pressure of 300 mm. Hg systolic and 180 diastolic. The urine showed nothing beyond a mere trace of albumin and some calcium oxalate crystals; the blood urea was 22 mgm. per cent.; the Wassermann and Kahn reactions negative. The retinae were normal, and pyelography of the kidney showed no trace of the drugs even after one hour of the injection. Nevertheless, the patient is feeling quite fit and has nothing to complain of. No drug or diet seemed to have any appreciable effect on his blood pressure. Could you let me know your opinion on the case as regards causation, prognosis and treatment?

REPLY.—I have discussed the case with some of my colleagues at the Central Middlesex Hospital. Both Mr. Fergusson and the radiologist are familiar with cases which have not shown any shadow of the kidney after pyelography on the first occasion, but subsequent examination has revealed normal outlines. It is certainly very uncommon but it can occur. It can be understood on the basis of the work of Trueta and Barclay, who have demonstrated the possibility of the cortex being by-passed under certain conditions and most of the blood passing into the medulla through the juxta-medullary glomeruli. It would seem necessary as the next step to repeat the pyelography and the blood urea estimation. If a normal renal function is demonstrated, the question of a Smithwick operation (dorso-lumbar sympathectomy) would be considered.

F. AVERY JONES, M.D., F.R.C.P.

hyperthyroidism. The following are the relevant points in the case.

May 2, 1944: Treatment begun with thiourea, 1 gm. daily. One month later the dose was gradually reduced on account of the satisfactory response.

June 6, 1944: Patient discharged from hospital with a maintenance dose of thiourea, 0.5 gm. daily.

November 20, 1944: On account of relapse, treatment changed to methyl thiouracil, 200 mgm. daily. There was again a satisfactory response, but it was found necessary to continue with 100 to 200 mgm. daily in order to maintain her in a state of full remission.

July 1945: Patient became pregnant.

August 1945: Recurrence of thyrotoxic symptoms, and treatment reinstituted with 200 mgm. of methyl thiouracil daily.

November 26, 1945: Methyl thiouracil stopped because of fear of possible toxic effects.

January 12, 1946: Treatment begun again on account of recurrence of hyperthyroidism, and 300 mgm. of methyl thiouracil was given daily, with only moderately satisfactory response.

March 28, 1946: Caesarean section performed fourteen days before term because of large and multiple myomas of the uterus. One month later the patient was symptomatic.

Thus, the total dosage before pregnancy was 109.5 gm. of thiourea and 21.8 gm. of methyl thiouracil, whilst during pregnancy she received 40.8 gm. of methyl thiouracil. At no stage of treatment did the patient show any signs of myxœdema. At birth the child was apparently normal and there was no enlargement of the thyroid gland. In the second month of life, however, the infant became very agitated and irritable, exophthalmos developed, and the blood cholesterol fell to subnormal levels. Only after a further two months did gradual improvement begin, and the exophthalmos had not fully disappeared eight months after birth. It is suggested that the mechanism involved was a blockage of fetal synthesis of thyroxine by the thiouracil, resulting in increased activity of the fetal pituitary gland which in turn was responsible for the symptoms. It is concluded that "administration of thiouracil derivatives to pregnant women demands caution and the child must be carefully observed".

The Complications of Mumps

A FOLLOW-UP of 208 cases of mumps after an epidemic in a military camp was carried out in order to estimate the occurrence of complications, and the results are recorded by D. Lawrence and D. McGavin (*British Medical Journal*, January 17, 1948, i, 94). Nervous complications occurred in the form of meningeal symptoms, headache, vertigo and vague aural symptoms. There were six cases of definite meningo-encephalitis among the men, and one case among the women. One man developed bilateral parotitis. Orchitis occurred in 53 cases, but there was no incidence of complete testicular atrophy and sexual activity was unimpaired. Some degree of pancreatitis was present in 16 cases, and one man complained of vague pain around the nipples. A thorough investigation of the cardiovascular system was not carried out,

but in 52 cases the pulse charts showed readings below 50. Among the women, in addition to the case of meningo-encephalitis, there was one case of secondary amenorrhœa for six months, and one case of mastitis. The remaining women patients mostly complained of tiredness, a complaint not made by any of the men.

A Barrier Cream

IN an article dealing with methyl cellulose (tylose M.50) in dermatological bases, R. E. M. Davies (*Pharmaceutical Journal*, January 31, 1948, 160, 82) includes a barrier cream which is undergoing clinical trials. The formula is as follows:—

R Liquid paraffin	10
Glycerin	10
Tylose M.50	6
Water	74

A gel is made by heating the water and adding the glycerin and while still hot this is mixed with the methyl cellulose gradually, mixing.

It is stated that the resultant cream forms an excellent "skin" on application. The substitution of liquid paraffin for part of the water of the jelly base increases the resistance of the film to sweat secretion. (Tylose M.50 is manufactured by Bayer Products Ltd.)

Edible Eggs

THE results of an investigation into the palatability of birds' eggs are reported by H. B. Cott (*Nature*, January 3, 1947, 161, 8). The following are the birds whose eggs were found to be palatable to man; among those listed in their order of palatability are:—

Domestic fowl, coot, moorhen, lesser black-backed gull, kittiwake, herring-gull, common tern, fulmar petrel, greater black-backed gull, guinea-fowl, razorbill, white-naped crane, chaffinch, hedge-sparrow, partridge, lapwing, spur-winged plover, stock-dove, jackdaw, spotted fly-catcher, domestic turkey.

The eggs of 15 species were found to be unpalatable, including the puffin, the blackcap, the ringed plover, the linnet, the great tit and the blue tit. The unpalatable eggs were described variously as acid, rancid, soapy, sour, oily, salty, fishy, and bitter. This last quality was the most important, and it was found most frequently among the species laying the smallest eggs. It is therefore suggested that this bitter quality may have been developed as a deterrent to potential egg-eating predators, especially as the assessments by experimental animals were in fair agreement with the human palatability rating. The five most distasteful eggs, those of the wren, the eastern house-wren, the blue tit, the great tit and the reed-warbler, were among the smallest tested. There also appeared to be an inverse ratio between palatability and conspicuousness of the egg. No close or obvious relationship was noted between the food habits of a bird and the flavour of the egg.

Nichols and F. R. Heilman (*Proceedings of the Staff Meetings of the Mayo Clinic*, December 10, 1947, 22, 561). Procaine penicillin G, a crystalline non-pyrogenic substance prepared by combining one molecule of procaine base (molecular weight 236) with one molecule of penicillin (molecular weight 334), resulting in a compound containing 41.5 per cent. procaine base, is stated to have a potency of 940 units per mgm., 90 per cent. of which is attributable to penicillin G, and a solubility in water at 28° C. of slightly less than 0.7 per cent. Ten patients, some ambulatory and some non-ambulatory, were given a single intramuscular injection of 1 c.cm. of an oil suspension of procaine penicillin G (300,000 units of penicillin), and the concentration in the blood was determined every three hours for twenty-four hours, starting three hours after injection. Except in one case adequate concentrations of penicillin were present in the blood twenty-four hours after injection, and in some cases for longer periods. Apart from slight pain at the time of injection there was no incidence of local irritation, soreness or pain after injection, thus suggesting that the procaine exerts a twofold action: (1) prolongation of the action of penicillin, and (2) an anæsthetic action. The conditions treated included septic sore throat, pneumonia, lymphangitis and carbuncle. No toxic reactions were noted.

The Spleen in Congestive Heart Failure

ACCORDING to N. O. Fowler (*Annals of Internal Medicine*, November 1947, 27, 733), "the spleen, on the average, is increased above the normal size in uncomplicated heart failure". This conclusion is based upon an investigation of necropsy material at the Peter Bent Brigham Hospital: 50 surgical cases used as controls, 50 cases of valvular rheumatic heart disease with congestive heart failure, 50 cases of hypertensive or arteriosclerotic heart disease, and 46 cases of subacute bacterial endocarditis. The average weight of the spleen in the different groups was as follows: surgical control group, 135 gm.; rheumatic valvular heart disease, 220 gm.; hypertensive and arteriosclerotic heart disease, 198 gm.; subacute bacterial endocarditis, 371 gm. Taking as his criteria that any spleen over 200 gm. is enlarged, and any over 300 gm. is clinically palpable, Fowler found that among 97 cases of uncomplicated congestive heart failure the spleen was theoretically palpable, i.e., over 300 gm. in weight, in 13.4 per cent., although in only one instance had the spleen been palpated during life. This splenomegaly of congestive heart failure did not appear

to be appreciably influenced by the duration of the failure or by the presence of infarcts. Another interesting finding was that in this series the spleen, on the average, showed greater enlargement than the average liver in congestive heart failure.

Sterosan Ointment in Mycosis of the Feet

DURING the bathing season mycosis of the feet is common, the infection being picked up at swimming baths, in bathing cabins and the like. A. Häfner and O. Kym (*Schweizerische Medizinische Wochenschrift*, December 27, 1947, 77, 1369) record the successful use of sterosan ointment in 27 members of a swimming club with persistent mycosis of the feet. The feet were bathed each evening with cold water and soap, and sterosan paste was applied to the interdigital spaces. The paste dries quickly, is not greasy, and adheres well to the skin. After 14 days, clinical and microscopical examinations were carried out in 25 cases, in 20 of which the fungus was found to be no longer present. In the 5 cases in which the fungus persisted the patients were free of pain, and one case became clear microscopically after further treatment. One patient did not continue with the treatment, and in three the infection persisted, whether as a residue or as a fresh infection could not be determined.

The Treatment of Plantar Warts

A SIMPLE and effective method of treatment of plantar warts is described by C. R. McLaughlin (*Lancet*, January 31, 1948, i, 168):—

Using a local anæsthetic, which is preferable as it minimizes bleeding, the overlying horny skin is pared down with a no. 11 blade until the bundles of the wart are clearly defined. A Volkmann spoon, the exact size of the wart, is then driven into the foot at the edge of the wart and swept round so that the core is removed in its entirety. The hyperkeratinized collar at the neck of the cavity is trimmed with scissors and the base scraped until smooth, and repeatedly touched with a diathermy needle or electric cautery, using a fine point, not too hot, with a light touch. Tiny satellite warts can be treated by boldly plunging in the diathermy needle, but any indiscriminate "frying" of the base of the large verruca must be avoided. A small wick of ribbon gauze is then inserted into the cavity and the area covered with gauze and Elastoplast. The patient can as a rule walk with care immediately, and there should be little discomfort forty-eight hours after the plug has been removed. Healing is usually complete in seven to ten days.

Thiouracil in Pregnancy

THE possible danger to the fœtus arising from the use of thiouracil derivatives in the treatment of hyperthyroidism during pregnancy is emphasized by A. R. Frisk and E. Josefsson (*Acta Medica Scandinavica*, Supplement No. 196, 1947). They report a case of an unmarried woman, aged thirty-five, who was found to have

practitioner. It is particularly suitable for house surgeons, if they can read German. Lüscher's book has a very full, well-arranged subject index, and has excellent illustrations, those of the eardrum in colour, done by the help of the otomicroscope, being especially noteworthy. Two very practical tables should be mentioned—one gives the old and new anatomical nomenclature, the other the salient features of the different forms of acute respiratory obstruction in children. Lüscher gives a guarded valuation to the operation of fenestration in otosclerosis.

Wayfarers in Medicine. By WILLIAM DOOLIN, M.B., F.R.C.S.I. London: Wm. Heinemann (Medical Books) Ltd., 1947. Pp. 284. Illustrations 39. Price 21s.

THIS volume consists of a series of essays by the distinguished editor of the *Irish Journal of Medical Science* which have been published in his own journal over a period of years. Written in that leisurely style which to the mere Anglo-Saxon is only a memory of the pre-war 1914 days, but which still characterizes the academic groves of Dublin, they cover the whole sphere of medicine from "the oldest physicians" to Sir Robert Jones. The book suffers from the inevitable drawback of any collection of historical essays, namely repetition, and it is to be regretted that the editorial blue pencil was not wielded more drastically. The only real criticism of the book, however, is that the author allows his religious views to bias his historical judgment, particularly in the days when the Papacy and the pioneers of medicine seldom saw eye to eye. As a bedside book, however, to be dipped into as a means of forgetting the harsh present in the historic past, the book can be thoroughly recommended.

NEW EDITIONS

A CHAPTER on chemotherapy in which the different sulphonamide derivatives and penicillin are discussed in detail has been added to *The Essentials of Modern Surgery*, edited by R. M. Handfield-Jones, M.C., M.S., F.R.C.S., and A. E. Porritt, C.B.E., M.Ch., F.R.C.S., in its third edition (E. & S. Livingstone Ltd., 50s.). Another addition is a short chapter on amputations. The new edition is beautifully produced and illustrated, containing in all 644 figures, some in colour.

The Conduct of Life Assurance Examinations, by E. M. Brockbank, M.B.E., M.D., F.R.C.P., in its second edition (H. K. Lewis & Co. Ltd., 12s. 6d.) has been rewritten in some sections to incorporate important changes in life insurance estimations. New data concerning expectation

of life, tuberculosis, cancer, hypertension and glycosuria risks have been included, with reports on the experience of insurance offices on these subjects. The practitioner will find much valuable information on the methods of examination for life assurance.

A Textbook of Clinical Neurology, by Israel S. Wechsler, M.D., in its sixth edition (W. B. Saunders Co., Ltd., 42s.) has been completely revised in order to include the many advances in neurology which have taken place during the twenty years since the first appearance of the book.

Clinical Studies in Psychopathology, by Henry V. Dicks, M.D., M.R.C.P., in its second edition (Edward Arnold & Co., 15s.) has not been submitted to any major changes: in the author's own words "psychopathology has not changed very much during the second war", rather have the views expressed by a small band of pioneers at the end of the stage of the emergence of psychotherapy after the first world war become more generally accepted. This book fills a niche of its own in psychiatric medicine.

Recent Advances in Sex and Reproductive Physiology, by J. M. Robson, M.D., D.Sc., F.R.S.E., in its third edition (J. & A. Churchill Ltd., 21s.) has been thoroughly revised and brought up to date in all sections. Artificial insemination, pregnanediol excretion estimation in the diagnosis of the non-ovulatory cycle and early pregnancy, the use of stilboestrol for inhibition of lactation, oestradiol inunction for promotion of growth of the breasts, and new information on the diagnosis and treatment of sterility are among the many new additions.

A SECTION on the treatment of otosclerosis by the fenestration operation, and another on penicillin are among the additions to *Diseases of the Nose, Throat and Ear*, by I. Simon Hall, M.B., Ch.B., F.R.C.P.Ed., F.R.C.S.E., in its fourth edition (E. & S. Livingstone Ltd., 15s.). This well-known textbook has been brought up to date in all sections.

Two new chapters have been added to *The Doctor and the Difficult Child*, by William Moodie, M.D., F.R.C.P., D.P.M., in its second edition (Commonwealth Fund: London; Geoffrey Cumberlege, 11s. 6d.), on treatment through play, and on the general organization of a child guidance clinic. In his preface the author discusses the problems created by evacuation and the breaking up of homes during and after the war.

REVIEWS OF BOOKS

Sir Frederick Banting. BY LLOYD STEVENSON, M.D. London: Wm. Heinemann (Medical Books) Ltd., 1947. Pp. xv and 446. Illustrations 23. Price 25s.

No medical discovery ever caught the public imagination more quickly and more completely than that of insulin. Not unnaturally the spotlight of publicity picked out the man primarily responsible for this dramatic culmination of generations of research into the problem of diabetes mellitus. Thus, almost overnight, Frederick Banting, hitherto a struggling Canadian surgeon known only to his colleagues and contemporaries, leapt into fame and became a name known throughout the whole civilized world. The professional career which began so dramatically ended equally dramatically, albeit tragically, when in 1941 Sir Frederick Banting was killed in an air crash while on his way from Canada to Britain. In his biography of Banting, Dr. Lloyd Stevenson has done full justice to his subject. Writing with intimate personal knowledge both of Banting and of his surroundings, he has been able to present a portrait of the man which rings true. Banting's was an enigmatic personality with strong likes and dislikes, and one of the great merits of Dr. Stevenson's book is the impartial way in which he has summarized the pros and cons of the unfortunate controversy which arose as to the relative precedence of J. J. R. Macleod and Banting in the discovery of insulin. The account of this vital episode in Banting's life, as well as that of his tragic end, could scarcely be bettered, but the method of dealing with the intervening years is not so satisfactory. For instance, practically nothing is said of Banting's private life. The long chapter devoted to extracts from his diary of a trip to the Hudson Bay Territory might well have been omitted to make way for a fuller account of Banting's home life. Written in an easy conversational style, this biography will appeal to both practitioners and laymen.

The Liver and Its Diseases. BY H. P. HIMSWORTH, M.D. Oxford: Blackwell Scientific Publications Ltd., 1947. Pp. xiii and 204. Figures 58. Price 18s. 6d.

IN this monograph, based upon the Lowell Lectures delivered at the Lowell Institute, Boston, Massachusetts, in 1947, Professor Himsforth surveys the mass of data now available concerning the liver, and has attempted to correlate the structural and functional pathology with the clinical manifestations of disease of this vital organ. After a preliminary chapter on the

types of liver injury and their structural consequences, he reviews the subject under headings of the vascular factor, nutritive factors and noxious factors in liver injury. Having then discussed the syndromes of hepatic failure, he introduces a proposed classification of liver disease. The final chapters are devoted to a review of the clinical aspects of the subject under the headings of his classification. This book, which is well documented and well presented, can be thoroughly recommended to clinicians, pathologists and research workers. The experimental outlook of the author is evident throughout the whole book, but even though this at times weakens the clinical character, it is a fault on the right side in these days when what is required above all for an understanding of liver disease is a hypercritical assessment of clinical data, and a more continuous application of the methods of clinical science to the problems of the liver in health and disease.

Chronic Structural Low Backache due to Low-Back Structural Derangement. I. R. A. ROBERTS, B.Sc., M.B., ChD, D.M.R.E. London: H. K. Lewis & Co. 1947. Pp. 105. Figures 137. Price 45s.

THE author has studied the problem of low backache from the anatomical, radiological and clinical aspects. The theme of the book is that the correct radiological interpretation of the films of the lumbar spine explains the onset of the clinical phenomena which have attracted attention since minor degrees of spondylolisthesis and prolapse of an intervertebral disc have been recognized. The case histories of 64 patients are described in detail. The illustrations are placed together and consist of reproductions of skiagrams and tracings, which are considered necessary to interpret the findings. It is a specialist book and controversial. The author discusses with great skill the points he wishes to make. Readers will take exception to some statements and arguments, and few will agree that a march fracture is not a fracture but an optical illusion. The 87 references, mostly from American journals, are useful and well chosen.

Kurze Klinik der Ohren-Nasen-und Halskrankheiten. BY ERHARD LÜSCHER. Basle: Benno Schwabe & Co., 1948. Pp. 513. Figures 201. Price Sw. frs. 54.

THIS short textbook of diseases of the ear, nose and throat is of ideal length for the student and

DIETETIC IDIOSYNCRASIES IN CHILDHOOD

By NORMAN B. CAPON, M.D., F.R.C.P.

Professor of Child Health, University of Liverpool; Physician, Royal Liverpool Children's Hospital, and Alder Hey Children's Hospital, Liverpool; Paediatric Physician, Liverpool Maternity Hospital.

THE term "dietetic idiosyncrasies" includes all types of unusual reaction which arise in relation to the taking of food. Some children are born with an idiosyncrasy for certain articles of diet and show an unexpected response when the particular foodstuff is taken. This state of sensitivity may be lifelong or may steadily decrease with time. Other children develop a temporary idiosyncrasy which presents difficulties in feeding for a limited period. Most of these dietetic idiosyncrasies, whether temporary or continued, are specific in the sense that by experience or testing a particular component of the diet is found to be the cause; and the manner of response that is evoked tends to be true to type. It is natural to look upon such reactions as manifestations of allergy, and there is no doubt that this is often true, especially when the offending foodstuff is a protein. But a dietetic idiosyncrasy is not invariably an allergic manifestation, and there are good reasons for restricting the term "dietetic allergy" to those examples in which a specific antigen-antibody reaction can be proved, or at least seems probable. Admittedly, the difference between idiosyncrasy and allergy may be difficult to establish in practice, and there are numerous cases in which the nature of the peculiarity remains uncertain.

But there are other examples of dietetic idiosyncrasy, usually less dramatic and therefore more difficult to recognize clinically, in which it would appear that the child is unable to tolerate quantities of certain foodstuffs (especially fats) which most children can digest and assimilate without inconvenience. In such cases the idiosyncrasy seems to be one of digestive incapacity or dysfunction rather than of specific sensitivity.

Finally, it will be necessary to call attention to examples of unusual behaviour shown by some children in respect of the act of feeding; for dietetics includes consideration, not only of the food that is taken, but also of the manner of its ingestion. It must, of course, be emphasized that children are liable to eat things which are not normal articles of diet, e.g., poisonous berries and toadstools, and when there is no knowledge that such substances

NOTES AND PREPARATIONS

MARMITE.—A new edition of "Marmite in Medicine and Dietetics" has recently been issued and contains some interesting tables showing the vitamin content and chemical composition of the product. A copy of the booklet can be obtained on application to the Marmite Food Extract Co. Ltd., Walsingham House, Seething Lane, London, E.C.3.

MOORE MEDICINAL PRODUCTS LTD., of Aberdeen, have opened a London depot at 64 Gloucester Place, W.1 (Tel.: Welbeck 5718), from where a prompt service for the supply and overhaul of Deedon inhalers for penicillin therapy is offered.

OXYGENAIRE LTD. have extended their day and night emergency service for oxygen tents and oxygen therapy equipment, which has already been in force for a number of years throughout London and the provinces, to cover Scotland, and is now available to all nursing homes, medical practitioners, and hospitals. Further particulars can be obtained from Oxygenaire (Scotland) Ltd., 8 Duke Street, Wigmore Street, W.1 (Welbeck 1322), or from 55 Deepdene Road, Westerton, Dumbartonshire (Bearsden 4373).

PUBLIC HEALTH CENTENARY EXHIBITION

In celebration of the Centenary of the first Public Health Act in Britain, a Public Health and Municipal Engineering Congress and Exhibition will be held at the Olympia, London, from November 15 to 20, 1948. The Exhibition, which has not been held for the past ten years, will include equipment for every branch of public service, medical, surgical and dental services, and municipal transport, thus illustrating the progress since the Royal Assent was given to the first Public Health Act in 1848.

PRIZES FOR NURSES

THE Council of the British Medical Association is awarding three prizes of the value of 20 guineas for the best essay, and three of the value of 10 guineas for the second best essay, on the following subjects:—"Suggested Improvements in the Methods of Training Nurses"; "Nursing the Patient, not the Disease—the Nurse-Patient Relationship"; and "Difficulties of Nursing in the Patient's Own Home and Their Solution". Those eligible to compete are pupil nurses, state registered nurses working in hospitals, and state registered nurses not working in a hospital. The essays must be forwarded so as to reach the Secretary of the British Medical Association not later than

May 31, 1948. Further particulars can be obtained on application to the Secretary, British Medical Association, B.M.A. House, Tavistock Square, London, W.C.1.

PUBLICATIONS

The Journal of Bone and Joint Surgery, vol. 30 no. 1, 1948, is the first British number of this important periodical. In future, alternate issues will be published in Britain, by an Editorial Committee representing the surgeons of the British Commonwealth, and in America. This number is distinguished by a buff cover bearing a portrait of Lister in contrast to the grey of the American issues, and it carries on its first page a gracious message of encouragement from His Majesty the King. Among its contents is a group of papers on recurrent dislocation of the shoulder with excellent illustrations, many of them in colour.

The British Orthoptic Journal, vol. 4, 1941 starts a new innovation in the form of contributions from ophthalmic surgeons and orthoptists practising overseas, which include an article on "What is Orthoptics" by W. J. Lancaster, M.D., of Boston, and one on "The Role of Orthoptic Treatment" by Miss Dore Mann of Melbourne. Communications concerning the journal should be addressed to the Editor (Mrs. E. Gwilt), Central Medical Establishment, R.A.F., Kelvin House, Cleveland Street, London, W.1.

The Health of the School Child: Report of the Chief Medical Officer of the Ministry of Education for the Years 1939-45, contains much useful information on the health of Britain's children during the war years, and the activities of the school Health Services during that period. The Report is published by H.M. Stationery Office at a price 2s. 6d.

The Almoner: A Brief Account of Medical Social Service in Great Britain, by I. F. Bedford A.M.I.A., opens with a foreword by Professor Alan Moncrieff, M.D., F.R.C.P., Nuffield Professor of Child Health, in which the important part played by the trained almoner in the medical social services is stressed. The vast scope of the almoner's work will be realized on reading this well-written monograph, which is published by the Council of the Institute of Almoners, Tavistock House (North), Tavistock Square, London, W.C.1, price 3s. 6d.

The contents of the April issue, which will include a symposium on "Minor Maladies of Childhood", will be found on page lxxiv at the end of the advertisement section.

feeding, and it seems probable that in this type of case a simple alimentary infection, or other temporary illness, may have been responsible for an abnormality of reaction which disappears again within a few days or weeks.

The introduction of *skin testing* raised hopes that the presence of any specific sensitivity might be revealed fairly easily and with considerable accuracy. The cases in which there is an undoubtedly positive reaction to a single food-substance are few, and the fact that the child possesses this specific sensitivity has usually been revealed unmistakably by the clinical history. More often the child who is suspected of sensitization is found to respond positively to a number of substances, most of which can be eaten without any obvious ill-effects. Skin testing for dietetic sensitivity is not valueless, but unfortunately it is a disappointing type of investigation. Intradermal testing is usually more accurate than the scratch test.

Elimination tests.—Greater help in elucidation of a suspected case can be obtained by elimination tests, various articles of diet being omitted one by one for a period during which clinical observation is maintained. When the patient is a breast-fed baby, it is reasonable to apply elimination tests to the mother's diet in order to discover whether or not the child has become sensitized to a protein, e.g. egg white, which is being eliminated in the breast milk. The foodstuffs which are most often concerned, in addition to human and cow's milk, are wheat, eggs and fish; sometimes orange juice, rice, nuts, chocolate, bananas and other fruit.

TREATMENT

The treatment of a dietetic idiosyncrasy depends upon the nature of the offending food and the degree of sensitivity.

Desensitization.—The infant who is markedly sensitive to either human milk or cow's milk presents a difficult problem. An attempt to desensitize the child by giving one drop of milk, diluted with water, on the first day, two drops on the second day, four drops on the third day, and so forth, may be successful but does not circumvent the problem of feeding during the period of treatment, which may take three months or more. Sometimes the symptoms are materially lessened when the milk is boiled for 30 minutes and the "skin" removed before being given to the baby. When this is not successful, a trial may be given to an evaporated milk or a specially treated dried milk, such as allergilac, or a milk substitute (Wolpe and Silverstone, 1942) which does not contain milk protein, such as *almata*.

The difficulties are less when the offending substance is not an essential component of the diet, or when the sensitivity is of slight degree. In these cases, the possibility of omitting the substance from the diet should be considered, because the state of sensitivity often disappears spontaneously after a few months or years. On the other hand, it is often better to persevere with the offending substance, especially if it is a valuable ingredient of normal diet, offering it in minute quantities at first, with a very gradual increase. For whilst it is true to assert that, for some adults, a

have been taken it may be thought that the toxic effects have been caused by an ingredient of the normal diet, or by the onset of some bacterial illness, such as gastro-enteritis. It would be outside the scope of this article to refer to these cases of poisoning, or to describe dietetic abnormalities due to organic disease of viscera.

FOOD IDIOSYNCRASIES

When a child is reputed to be unable to tolerate a certain article of diet it is well to inquire into the feeding habits of the family and to conjure up a mental picture of the conditions under which the particular food has been offered. For instance, when the parents are food-faddists the child is likely to be moulded in the same pattern, and even if he does not vomit a food which is offered with misgiving, he will be likely to develop an unreasonable distaste for it. Within a very short time one hears that "it does not suit him"; or "it gives him spots"; or "he always seems to get indigestion after taking it". In such circumstances there may be difficulty in deciding whether or not the child really shows an idiosyncrasy for the particular foodstuff; and the true nature of such cases may be revealed when it is found that during the first term at boarding school the child's peculiar reactions ceased.

Again, some infants appear to be influenced by the facial grimaces of a mother who offers a foodstuff, e.g. cod-liver oil, which she herself dislikes because of the taste or smell; these babies may spit the stuff out, or vomit, and they may speedily acquire the reputation of being unable to tolerate the particular article of diet.

FOOD ALLERGY

It is unusual for a specific dietetic sensitivity to appear as a familial characteristic; more often it is peculiar to the individual, and in some cases the state of sensitivity has arisen during antenatal life, thus providing an interesting example of maternal threat to the foetus. For instance, there are rare cases in which the contact of a few drops of the mother's milk may cause the infant's lips to swell, and within a very short time there may be projectile vomiting, dyspnoea, and the appearance of a generalized rash, usually either erythematous or urticarial in type. More often, the offending substance is contained in a food other than human milk, and although the immediate effect may be no less dramatic in onset, the symptoms are frequently somewhat indefinite, and may be incorrectly ascribed to other causes, such as bacterial infection producing gastro-enteritis. Nausea, vomiting, diarrhoea, abdominal pain, fretfulness, unsatisfactory gain in weight, urticaria, infantile eczema, and flexural dermatitis are the more common clinical manifestations, but sometimes paroxysmal sneezing, congestive rhinitis, rhinorrhoea, purpura of the Henoch type, and acute asthma are seen. Some examples of the fatigue syndrome may be due to dietetic allergy (Radolph, 1947). It has been mentioned that a state of sensitivity may develop in a child who previously has not shown any abnormal response to

UNUSUAL FEEDING BEHAVIOUR

The feeding-pattern of children may be influenced not only by mental and physical disease but also by the form of their management. For example, some children acquire a greedy and precociously selective appetite when they are indulged and pampered by their parents; others—and this is especially true of “only” children—are liable to develop negativism in respect of feeding when a great deal of attention is centred upon their performance at meal times by parents who are conscientious and somewhat unstable. Such children refuse their food and every meal develops into a “scene”, in which the worried parents ring the changes on persuasive encouragement, bribery, and angry command in their attempts to make the child eat. Widdowson’s (1947) study of children’s diets brought out a fact well known to pædiatricians, namely that similar children may differ enormously and unpredictably in their food habits; and parents who try to make their children conform to a certain pattern (usually set by a child relative of large appetite) run the danger of causing unnecessary and unhealthy conflicts. Although it is true that many children who are negativistic to feeding continue in good physical condition despite their unwise management, some become subnormal in weight and height, and it has been suggested (Talbot, *et al.*, 1947) that emotional disturbances which result in a low intake of total calories may thus give rise to a functional hypopituitarism as an adaptive reaction to the state of malnutrition.

There may be much difficulty in correcting faults in management, and the practitioner must first satisfy himself that the child is not suffering from any organic disease of body or mind. When that is done, he should explain the situation in terms which the parents can understand, and advise them to make a gradual reduction of the amount of food offered to the child, and to show no anxiety at meal times. Gradually the appetite will return—an essential condition of normal alimentation in childhood—and progress is then satisfactory. When it seems obvious that the parents will not be able to carry out this advice the child should be placed temporarily in a residential nursery, home or school, in order to protect him from the over-anxiety of parents and to give him the example of children who feed normally.

Conclusion.—There is ground for believing that some of the present widespread propaganda upon health matters has an undesirable effect upon parents whose sense of responsibility is not accompanied by a common-sense, well-balanced outlook. For optimal development, both of mind and body, there must be a certain latitude for experiment (trial and error), and difficulties are likely to arise when adults neglect this natural law and try to confine the child strictly to a definite, narrow path.

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dietetic idiosyncrasy constitutes a harmless means of self-expression, and its removal, if this were possible, would leave a void which would probably be filled by the development of some other personal peculiarity, children should not be encouraged to harbour susceptibilities which make them conspicuously different from their fellows. This is not to say that in childhood individualities should be suppressed; but the development and maturation of both mind and body during childhood are best encouraged when the individual lives a full life within the social pattern appropriate to his age-group, and this is seldom possible if he differs conspicuously from his fellows in the routine of everyday life.

An acute attack of dyspnoea due to food allergy may be controlled by adrenaline or by benadryl, the latter being given in a dosage of 2 mgm. per lb. of body weight daily, divided into three or four doses in the twenty-four hours.

RELATIVE INTOLERANCE FOR CERTAIN FOODSTUFFS

It is more than likely that there are children who have a relative intolerance for protein or for carbohydrate, but these cases do not seem to be of much practical importance. On the other hand, relative intolerance for fat is fairly common in a certain type of child and often causes symptoms. The subjects of this condition are generally intelligent, highly strung, thin children of intellectual parents whose anxious desire to perform their full duties is carried to a fault. The patient, often an only child, is offered a diet which contains more fat, e.g. butter, eggs and creamy milk, than can be tolerated, and when necessary the parents resort to persuasion or even disciplinary measures to ensure that all the food is eaten. Indigestion is likely to develop and the child may then have a coated tongue, offensive breath, apathy, pallor, irritability of temper, and fleeting abdominal pains, especially at meal times or just after food. The motions are often pale, loose and mucoid. In some cases there may be headache, nausea and prostration—thus *simulating migraine*—followed by vomiting, pyrexia, abdominal pains, a sweet odour in the breath, and the passage of urine containing large quantities of ketone bodies. There can be no doubt that mental excitement, anxiety or shock may be intimately linked with the syndrome, and after the acute illness has been overcome the child's return to a normal state of health will be encouraged by the establishment of environmental conditions which reduce nervous tension; for instance, when the adults in charge are unrelated to the child and are themselves well-balanced, sensible and placid. This aspect of the treatment is perhaps the most important; common-sense management and the encouragement of the child's self-confidence. Obviously it is reasonable to make some reduction of the fat in the diet; milk may be skimmed, butter should be sparsely used, and not more than two eggs weekly should be taken. Fried fat is best prohibited for a time. But it is unwise to forbid fat entirely, because this may encourage the child to grow up "food-conscious".

A triad may be produced of *local itching, restless sleep, and irritable tiredness*. It is possible that vague gastro-intestinal disturbances are due to oxyuriasis, but they are as likely to be due to remedies given for the worms; and there is no evidence that threadworms cause appendicitis, enuresis, nose-picking, poor appetite or fits. However, many mothers are distressed by the discovery of these minute animals; and practitioners and other health workers can do much to diminish this anxiety.

THE METHOD OF SPREAD

Oxyuriasis is only acquired, directly or indirectly, from other human cases. The eggs from the source of infection are ingested and swallowed. They contain larvæ which hatch out in the duodenum, develop and mate. This is the climax and end of the male worm's life, but the female continues to develop and travel downwards, reaching the colon in four to six weeks. As with all nematodes, the ova cannot develop into adults unless they leave the host. The threadworm is unique in that when fully mature and containing 10,000 to 15,000 ripe ova, the female emerges at night from the anus to lay these eggs on the perianal skin and die.

The eggs are small and light and spread easily from the perineum to the bedclothes and clothes of the host; and thence they become widespread as he moves about. Schüffner (1944) found 305 eggs per square foot of surface in classrooms. Nolan and Reardon (1939) found ova in 221 of 241 specimens of dust from houses of infested persons, half the ova being viable. Working on dust from a children's out-patient department and from the homes of oxyuriasis cases we found ova in a far lower proportion of our 200 specimens, but infection or reinfection from house-dust remains a very real possibility.

DIAGNOSIS

If a hundred cases were investigated by microscopic examination of the stools, about one case would be detected. If stool flotation methods were used, ova might be found in ten of the hundred. The newer methods of recovering ova from the perianal skin are far more reliable and, if repeated tests are done, 90 to 100 per cent. may be diagnosed. If seven tests made over a fortnight are negative, a subject may be pronounced free of oxyuriasis.

The first of the new techniques was the NIH swab described by Hall (1937). This was a great advance but is rather inconvenient to prepare and to examine. After doing exhaustive studies of the efficiency and convenience of different methods, we consider that the pestle (Schüffner and Schwellegrebel, 1943, 1944), and the adhesive cellulose tape (Graham, 1941) are the most generally useful methods (Watson and Mac Keith, 1947a, b). These two methods are illustrated in figures 1 to 12.

The pestle test is cleanly and gives an easily examined specimen; the cellulose tape technique is more simple but, until the observer is used to it, the eggs are rather more difficult to identify. Both methods have been found

THE DIAGNOSIS AND TREATMENT OF THREADWORM INFESTATION

BY RONALD MAC KEITH, D.M., M.R.C.P.
AND JOHN M. WATSON, D.Sc., A.R.C.S.

*From the Department of Child Health, Guy's Hospital, and the Wellcome
Laboratories of Tropical Medicine, London.*

"The other lesse sorte (of worms) . . . may wel be knownen by the excedyng ytche in the fundament within": *Thomas Phaer*, 1544.

"But though all these signs are usual in cases of worms, yet they are sometimes met with where there are no worms; and at other times worms are voided without any previous notice": *William Heberden*, 1807.

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A NOT uncommon arrival in the surgery or out-patient department is a mother who says she has given her child worm capsules from the chemist but the threadworms are still there and what can she do? She is probably needlessly disturbed, and it will be well to begin by telling her that she may be glad to know that, although sometimes very annoying, threadworms never produce any serious illness. If the mother will describe any worms she has seen, a guide to the right diagnosis may be obtained by discovering the "threadworms" are "as big as a pencil" or "are only present after the child has eaten bananas".

INCIDENCE

Eleven years ago the National Institute of Health of the U.S. Public Health Institute started an extensive team research on oxyuriasis which has given much information and stimulated many other studies. The incidence of infestation with threadworms in various groups has been found to be from 7 to 95 per cent., being lower in adults and in negroes. When one member of a family is infested it is usual for others, including adults, to be affected also. In London we found that 40 to 50 per cent. of child in-patients and out-patients are infested, and in one small residential boys' home 100 per cent. were heavily infested. We have not yet been able to determine the incidence in adult groups in this country.

SYMPTOMS

In the above boys' home none had symptoms, and in our experience less than one in twenty of those infested have symptoms indubitably due to the parasite. Nor is the incidence of symptoms related to the heaviness of infestation; it apparently depends more upon the personality of the subject.

The cardinal symptom, *pruritus ani*, seems to be due to worms in the rectum or anal canal rather than on the perianal skin. Oxyuriasis is probably the most common cause of *pruritus ani* in grown-ups, as well as in children.

A triad may be produced of *local itching*, *restless sleep*, and *irritable tiredness*. It is possible that vague gastro-intestinal disturbances are due to oxyuriasis, but they are as likely to be due to remedies given for the worms; and there is no evidence that threadworms cause appendicitis, enuresis, nose-picking, poor appetite or fits. However, many mothers are distressed by the discovery of these minute animals; and practitioners and other health workers can do much to diminish this anxiety.

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G THREADWORM EGGS

B. GLASS PESTLE (SCHÜFFNER AND SCHWELLENGREBEL, 1943-44)

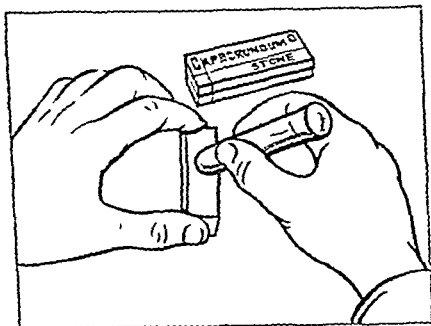


FIG. 7.—To prepare the pestle, the rounded tip of a thick glass test tube is roughened on a carborundum stone or wheel.

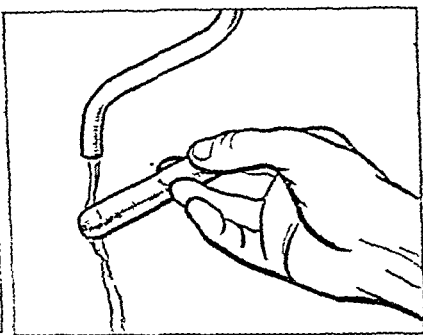


FIG. 8.—Dip the tip of the pestle in clean water.

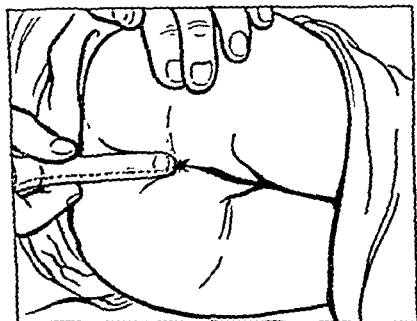


FIG. 9.—Rub the pestle on the skin around the anus for ten seconds (not into the anus).

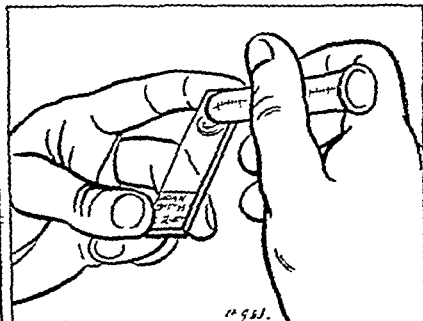


FIG. 10.—Transfer the emulsion of epithelial cells and ova on to a labelled glass slide.

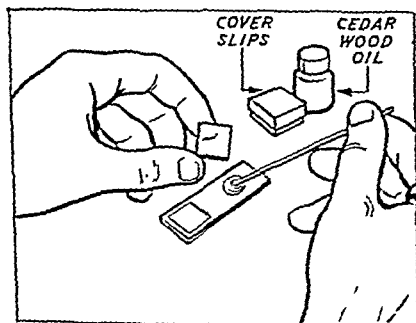


FIG. 11.—On the dried slide add a drop of cedar-wood oil and a coverslip.

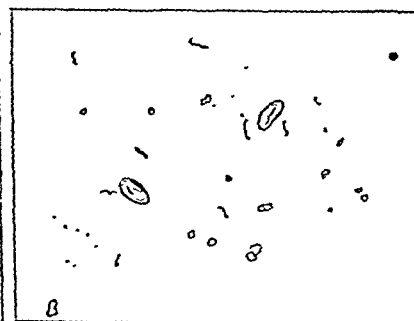


FIG. 12.—Examine under the low power $\frac{2}{2}$ -inch objective lens.

Although the preparation may be examined wet, it is more simple to allow it to dry and examine it at leisure.

TWO METHODS FOR

A. ADHESIVE CELLULOSE TAPE (GRAHAM, 1941)

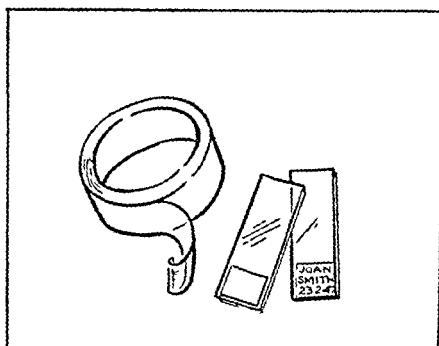


FIG. 1.—Roll of 1-inch wide adhesive cellulose tape and glass slides to be labelled with name and date.

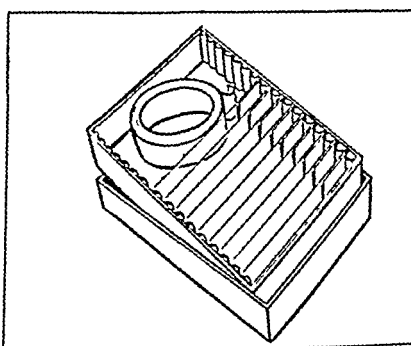


FIG. 2.—A box with slides and tape as supplied to parent or patient to take seven slides during a fortnight.

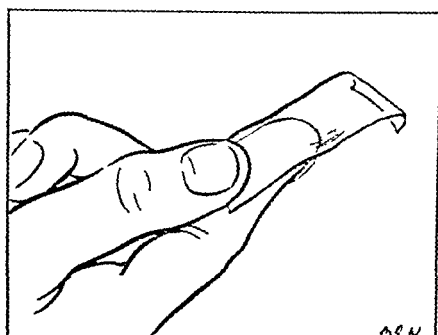


FIG. 3.—From the roll tear off a 2-inch length of tape.

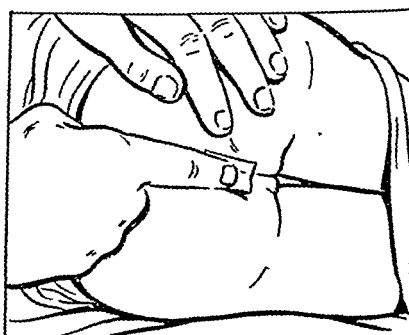


FIG. 4.—With the forefinger apply the sticky side of the tape to the perianal skin; remove it, and—

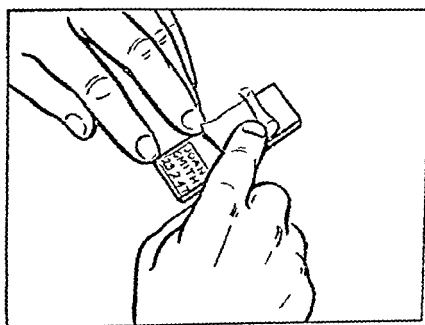


FIG. 5.—then stick the tape carefully down on to a labelled glass slide, pressing the tape down with the finger to exclude air bubbles.

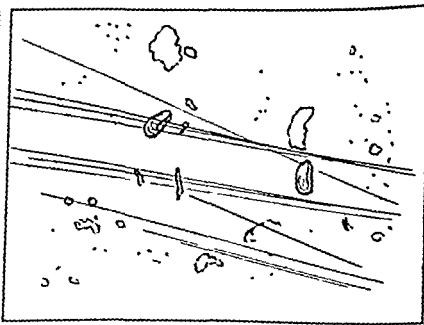


FIG. 6.—Examine under the microscope for ova, which may be picked out with $\frac{5}{8}$ -inch objective and confirmed with a $\frac{4}{8}$ -inch lens.

worms will be removed before they are mature, and hence before the ova are infective. In this way reinfection will be impossible whatever the habits of the subject.

It is evident that a combined attack from above and below may be the most successful. Some mothers will already know how to give enemas; others will learn easily from the district nurse; in many cases it will be necessary for the nurse to give all the enemas. Before giving a detailed plan for treatment it is worth recalling that the remedy should not be worse than the disease. After all, threadworm infestation is usually symptomless and even pruritus ani is not fatal. One fatality (see *Lancet*, 1942) and several cases of toxic anæmia have followed treatment with phenothiazine for oxyuriasis. Apart from such risks, the side-effects of drugs, such as abdominal discomfort from gentian violet, the nuisance of any complicated system of treatment especially when the whole household are expected to cooperate and, finally, the unhappiness produced in mothers and children by a threadworm neurosis, must all be taken into consideration.

Plan for treatment.—The investigation of oxyuricides takes much time, and there are many cases yet to be tested by methods giving true criteria of efficiency. Our results to date with the reports in the literature lead to the following suggestions for treatment:—

(1) A specific treatment for the pruritus ani is a small enema of 2 or 3 ounces (55 to 85 c.cm.) of tap water. Occasionally this will remove the only worms present and give lasting relief. In any event it will give an undisturbed night's sleep.

(2) Before embarking on further more prolonged treatment, it is wise to review the diagnosis and decide whether treatment is worth while.

(3) In all cases, *hygienic measures* must be practised as well as therapy by drugs.

(i) Pyjamas or knickers should be worn in bed.

(ii) On rising, the perineum should be washed with soap and water and thoroughly rinsed (if houses in this country had bidets, as are common on the continent, this item would be facilitated). The patient should have a towel for his own exclusive use, and should use no other.

(iii) The hands should be washed before meals.

(iv) Ointment may be applied to the perineum if desired. The nature of the ointment is unimportant as the chitinous shell of the ova is quite impervious to all toxic agents, but benzocaine ointment may be tried if there is pruritus.

(v) During the course of treatment the bedclothes and the clothing should be changed and washed or dry cleaned.

(4) For the first time of treating a case, gentian violet in enteric-coated tablets may be used. The dose is $\frac{1}{18}$ grain (3.5 mgm.) for every year of age, up to a maximum dose of 1 grain (65 mgm.), three times a day for seven days, followed by a week's interval and then a second course for seven days.

The tablets are given after meals. The patient should be warned not to bite the tablets and that the motions will become black. Toxic symptoms are uncommon in our experience; sometimes there is abdominal discomfort or nausea. This often stops, even if the drug is continued, and ceases if the drug is omitted for a day or so.

When gentian violet is declined or is known to give toxic symptoms,

straightforward enough to be used by parents of children attending out-patient departments.

TREATMENT

In a proportion of cases, oxyuriasis causes an "ytche in the fundament" which may be very trying indeed. In such cases, treatment is necessary. But it is worth while to review the therapeutic resources before deciding on the treatment of cases with occasional mild pruritus, symptomless cases in which live worms have been seen in the stools, or cases detected by improved diagnostic methods.

The time taken for the parasite to travel from mouth to anus and to grow from an egg into a mature worm full of developed ova is four to six weeks. Ova cannot develop without leaving the host's alimentary canal. Hence, if reinfection is avoided for some six to eight weeks the infection will die out. Hygienic measures by themselves should lead to cure, and they certainly should never be neglected. For one thing, when pruritus is present, transfer of eggs on the fingers may easily convert a light infection into a heavy one. But in practice, by themselves hygienic measures are not a reliable method of treatment. D'Antoni and Sawitz (1940), in a residential school, instituted a thorough attack on these lines for six weeks with no diminution but an actual rise in the percentage infested.

To eradicate the infestation a treatment is needed, vermicide or vermifuge, which is 100 per cent. efficient, which does not give symptoms worse than the disease, and which is applicable to all members of the household. Furthermore, it should be possible to give the treatment over a period so that the ova present in the house-dust when treatment is started have time to die before treatment is completed, for otherwise reinfestation is probable.

As regards *treatment by drugs* given by mouth, it is well to quote what was said by Andry in 1701, in discussing this problem:—

"Threadworms are difficult worms to eradicate, and this for several reasons. The first is that these animals are a long way from the stomach, so that remedies lose their effect before reaching where the worms are. The second is that the threadworms are enveloped in thick mucus which hinders the action of drugs. The third is that these worms sometimes stay in the cæcum; now, this part of the bowel being a cul-de-sac, the threadworms stay there cut off, so it may be more useful to attack them from below".

It is difficult to resist a further quotation from Andry in 1701:—"For children, this is the washout that one may use:—Take leaves of mallow and of violets and gillyflowers, of each a handful; cabbage leaves, one or two; seeds of coriander and fennel, of each 2 drachms; flowers of camomile and of little centaury, a pinch of each; make a decoction of all with milk and dissolve in the filtrate an ounce of common honey, and 2 drachms of confection of beetle".

It would seem preferable to avoid the use of enemas, but no one who has seen the immediate relief that results from a small enema given in a case of severe threadworm pruritus will deny the usefulness of such treatment at times. Indeed, this has been a valuable diagnostic test in cases of pruritus ani in adults. If reinfection from above is avoided and the worms are cleared from the lower bowel by enemas given once or twice a week, then the

ADIPOSIITY IN CHILDHOOD

By RAYMOND GREENE, D.M. M.R.C.P.

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THERE is no reason to believe that the causes of adiposity in children differ essentially from those in adults. The subject is of separate importance only because of the light thrown upon the whole subject by a few special cases, of which the most important are Fröhlich's syndrome and the Laurence-Moon-Biedl syndrome, both of great rarity but of an academic interest surpassing their practical importance. It is as well to confess at once that the cause of obesity is as yet unknown. The various hypotheses which have been advanced have been severally demolished (Greene, 1946), but as a few of them are still quoted, lifting their heads like so many spurious phoenixes from their ashes, it is as well to summarize them briefly.

(1) That obesity is due to *overeating*. This hypothesis is a result of false deductions from the law of the conservation of mass. A little experience soon shows that there are fat people who eat too much and others who eat very little, and thin people who are just as gluttonous and as restrained. This still leaves unanswered the question why some people who eat ravenously remain thin whilst others who eat little still grow fat.

(2) That fat people have a *low basal metabolic rate* due, it is often assumed, to thyroid deficiency. In fact, the basal metabolic rate of fat people is not abnormal. This accounts for the comparative inefficacy of thyroid extract in the treatment of adiposity. Thyroid extract in small doses has, as will be seen later, some slight value, probably in virtue of its diuretic action. Apart from this diuretic action it is valueless unless given in doses sufficiently large to induce a temporary thyrotoxicosis. This is a dangerous procedure: permanent thyrotoxicosis may be induced.

(3) That fat people have a *low specific dynamic action*. Experiments have failed to confirm this. Indeed, the variations of the specific dynamic action of food in normal people are so great that nothing short of its complete absence can be considered abnormal.

(4) The hypothesis of *luxuskonsumption*. Gräfe and Grünthal (1929) sought to show that a high intake of food produces an increased metabolism over a long period, whereas a low intake reduces the metabolic rate. The hypothesis is only half true. Although starvation does in fact diminish the basal metabolic rate, the opposite is not true.

(5) That there is a *disorder of absorption*. The examination of the faeces shows that this is not the case, the residual calories bearing no relationship to the obesity of the individual.

(6) That there is a *constitutional abnormality of adipose tissue*, which hangs on to the fat and prevents its use as fuel. At first sight this hypothesis has much to recommend it, but it does not bear the test of experiment. The opposite is apparently the truth.

THE ENDOCRINE GLANDS

A different approach to the problem is offered by a consideration of the part which may be played by various organs in the production of obesity. It is fashionable to inculcate the endocrine glands and even to apportion the blame in accordance with the distribution of the fat, some so-called

diphenan may be given instead. It is supplied in tablets of 7.5 grains (0.5 gm.), and is given three times a day for a week, repeated if necessary after a week's interval. The dose for infants is one $\frac{1}{4}$ tablet; for children of one-and-a-half to ten years, $\frac{1}{2}$ a tablet; for children over ten or adults, 1 to 2 tablets, given in each case three times a day after meals.

(5) If the infestation and symptoms recur, the next step is to give the gentian violet treatment to the whole household.

(6) The next line of treatment is gentian violet by mouth combined with enemas of hexylresorcinol. A retention enema is given of 5 to 10 ounces (125 to 250 c.cm.) of a 1 in 2000 solution of hexylresorcinol. This is a saturated solution. Six to ten enemas are given, preferably in the evenings, during the three weeks of the gentian violet treatment.

Alternatively, hexylresorcinol may be given by mouth once a week for five weeks, in combination with the enemas. It may be obtained as caprokol in enteric-coated tablets of 0.2 gm. The dose for children up to five years of age is 0.2 to 0.4 gm.; four to ten years, 0.6 to 0.8 gm. It is given fasting with a glass of water and no food for four hours.

These methods of treatment give a reasonable chance of relief of the condition. They are not the only ones, but to quote Hieronymus Mercurialis (1584): "Many other remedies have been traditionally recommended by doctors for worms which I will not, however, discuss in this place".

We are glad to have the opportunity to thank, among others, Miss Eve, S.R.N. and Miss Rains, S.R.N., Miss Atkins and Mr. J. Judd; Drs. MacMahon, Sheehan and Arthurton, and Mr. O. D. Standen, M.Sc.

The figures are drawn by Miss M. J. Waldron of Guy's Hospital Illustration Department, from photographs taken by Dr. B. Stanford for the filmstrip "The Diagnosis of Threadworm Infestation", published by Unicorn Head Filmstrip Library, 177 The Vale, Acton, London, W.3.

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and the eunuch of the Eastern harem is always represented as of enormous corpulence. On the other hand, the typical hypogonad male is tall and thin. Skopecs, who are castrated before puberty, are not necessarily fat, and obesity does not necessarily follow the castration of adults. It seems likely that when obesity does occur it is because of the diminished activity of castrates, with perhaps a transference of interest from sex to the pleasures of the table. Similarly in women, oöphorectomy and the menopause are commonly, but not invariably, followed by a varying degree of adiposity.

THE HYPOTHALAMUS

Recently attention has shifted from the endocrine glands and has become focused on the hypothalamus. It has been recognized for many years that tumours in or near the base of the brain, or encephalitis affecting this area, may cause obesity. Moreover, obesity may be caused by experimental damage to the hypothalamus of animals. The exact part of the hypothalamus concerned is still uncertain. The experiments of Bailey and Brémer (1921), Gräfe and Grünthal (1929), Smith (1927) and Hetherington and Ranson (1939) point to the neighbourhood of the tuber cinereum. The importance of these observations on the fat-regulating centre achieve an increased interest by reason of the association of obesity with disorders of water metabolism and of sex, both of which are primarily hypothalamic functions.

The association of obesity with actual pitting œdema of the shins is hardly mentioned in textbooks of medicine. The average student is taught to regard œdema as a sign of renal or cardiac disease, although in these days he may have learned enough from real life to give a passing thought to beri-beri and the low plasma proteins of starvation. In fact, the majority of very adipose patients show this sign to a greater or lesser extent. When it is remembered that an increased water content of many pints must be present before pitting can be produced, it is natural to wonder if water retention is not a constant factor in adiposity (Greene, 1946). It may be that some cases of so-called obesity are in fact due to water retention rather than to fat retention. The Volhard water test often shows fluid retention in obese patients; but of greater importance are the results of clinical observation during treatment. The occasional complete failure of a low calorie diet to produce any significant fall in weight in fat women during the first few weeks of treatment by such means alone is an impressive fact. The combination of such a diet with a diuretic and the restriction of fluids produces rapid results.

The nucleus supra-opticus of the hypothalamus is well known to operate its control over water metabolism by way of the posterior pituitary, and the posterior pituitary by way of the kidneys. A flood of light has been thrown on the whole subject of water retention in adiposity by the work of Verney and his collaborators (1935, 1938, 1942), who have shown that under the influence of anxiety the urinary flow of dogs is diminished, with consequent

types of obesity being described as "pituitary" and others as "thyroid", "gonadal", and so forth. I believe there is no basis for any such classification. The only exception which is worthy of consideration is Cushing's syndrome, and even in this disorder the connexion between the typical distribution and the pituitary is suspect.

The part played by the *anterior pituitary* in the production of obesity has been grossly exaggerated. It would, perhaps, be too dogmatic to say that the anterior pituitary has nothing whatsoever to do with obesity, for against such an assertion is the doubtful example of Cushing's syndrome (which, by the way, is a *hyperpituitary* condition) and also the observation of Keller *et al.* (1935, 1936, 1937) that obesity occurring after hypothalamic lesions may be diminished by hypophysectomy. The latter observation is contradicted by the later experiments of Hetherington and Ranson (1942) and in any event cannot logically be cited as a proof of anterior pituitary participation in the preceding obesity. Whatever the truth may be, it may be said categorically that no known preparation of the anterior pituitary, given by any route, is of the slightest efficacy in obesity of any kind. The *posterior pituitary* has, on the contrary, been neglected. Overaction of this gland—not deficiency—is probably, as will be seen later, of considerable significance.

The rôle of the *thyroid* has also been exaggerated. In any examination a large proportion of students will cite obesity as one of the cardinal symptoms of hypothyroidism. An increase in weight is, in fact, usually seen in myxœdema, but this increase is due not to fat but to water, and to the mucin laid down in the tissues. The increase is not usually great. Patients with severe hypothyroidism are often thin. Adiposity and hypothyroidism are both common at the climacteric and this has created a false impression. Numerous experiments on animals and clinical observations on men and women have shown that hypothyroidism does not of itself produce obesity (Greene, 1946).

The *adrenal cortex* may possibly have an important bearing on the problem. Patients suffering from Addison's disease are always thin, and those with adrenal hypertrophy are often, though not invariably, fat. Whereas adrenalectomized rats lose all their body fat, both normal and adrenalectomized rats gain weight when cortical extract is injected. These facts may be explained in two ways. In the first place, in adrenal deficiency carbohydrate is not formed from protein, so that all available carbohydrate is needed for energy production and none is stored as fat. In the second place, the injection of cortical extract causes a fall in blood lipoids owing to these being taken up by various tissues, especially the reticulo-endothelial system. The experimental findings are confused, but it is possible that fat is more rapidly taken up by the adipose tissues of those whose output of cortical hormone is high.

The part played by the *gonads* is also difficult to interpret. Castration is, of course, regularly practised with a view to fattening animals and birds;

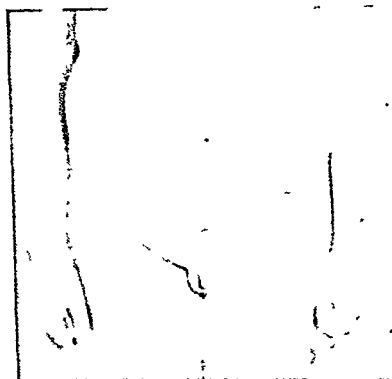
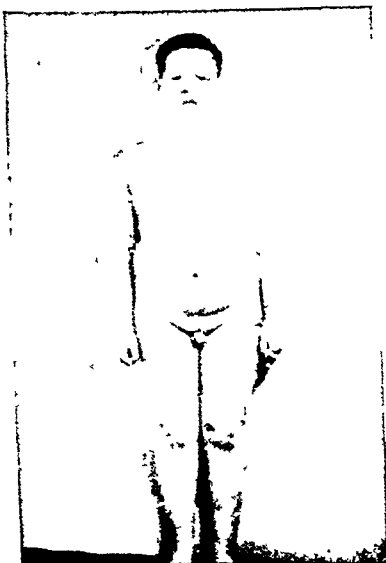


FIG. 1a.—Case of infantile obesity, wrongly diagnosed as Frohlich's syndrome. Age 11.

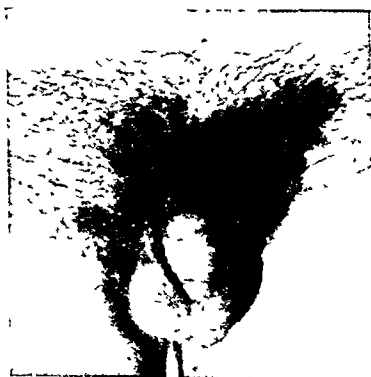
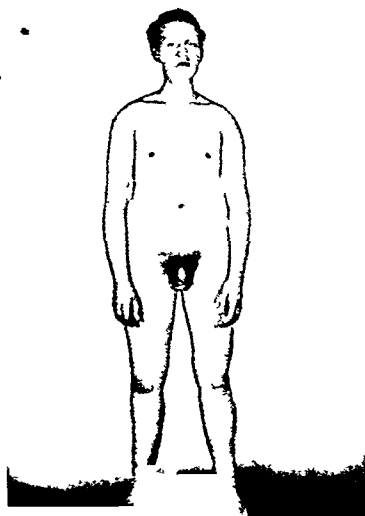


FIG. 1b.—Result of treatment with restricted carbohydrate. No endocrine treatment given. Age 18.

water retention. I have reported (Greene, 1946) that a similar phenomenon occurs in man, and that anxiety does not necessarily, as is usually supposed, cause a fall in weight. It commonly produces adiposity with pitting œdema. Since my article was published I have collected numerous examples, but as all have been adult I will not now describe them in detail. There is no reason to suppose that the phenomenon does not occur in children. That anxiety is a potent factor in the production of obesity in children has been pointed out by Hilda Bruch (1939c, 1940b).

Bruch's factual studies have added greatly to our knowledge. She has established (1939a), as others had already for adults, that there is no reason to believe that thyroid deficiency plays any part in the obesity of children and that thyroid extract in a safe dosage is valueless in treatment; that the future development of the majority of such children is normal (1939b); that their energy requirements during muscular exercise are normal (1940a); that their muscular activity is, however, generally less (1940a); and, most important of all, that emotional factors play an important part in the development of their adiposity (1939c, 1940b).

Bruch produces much evidence that in a high proportion of fat children in the United States a degree of emotional immaturity is present: 35 per cent. of her subjects were only children, and another 35 per cent. over-protected younger children. The majority were late in acquiring the ability to look after themselves, and in 40 per cent. enuresis occurred. In at least 80 per cent. there was evidence that the food intake was above the normal. In common parlance, we may say that most of her patients were spoilt, lazy and gluttonous little brats, with a deficiency in parental discipline rather than in glandular secretion.

It would indeed appear that alimentary obesity is more common in children than in adults, but it is improbable that a mere excess of income over expenditure is the sole explanation in more than a small proportion of cases seen in this country. Bruch indeed suggests that emotional causes bring about obesity by way of the hypothalamus, and quotes cases of the sudden onset of adiposity after operations, severe illnesses and the death of relations. Because mere gluttony is certainly not as common a cause in this country as in Bruch's American series, this small group of sudden onset acquires a particular significance. I have no doubt from a study of my own series that, in Britain, anxiety is an important factor in the production of adiposity in adults and to a lesser extent in children, and I differ from Bruch in that I have failed to establish that the mental condition has produced the physical condition by increasing the appetite. I believe that in such cases the greater part of the increase in weight is due to water retention rather than to the laying down of fat. The mechanism is that described by Verney and his collaborators (1935, 1938, 1942). Anxiety leads to a change in the function of the hypothalamus (as Bruch, indeed, admits), which causes an increase in the output of posterior pituitary hormone and a consequent decrease in the output of urine. The same mechanism is brought into play when the hypothalamus is damaged by other agents.

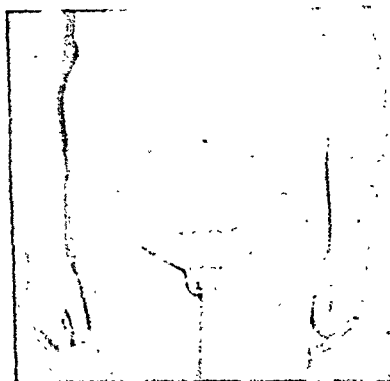
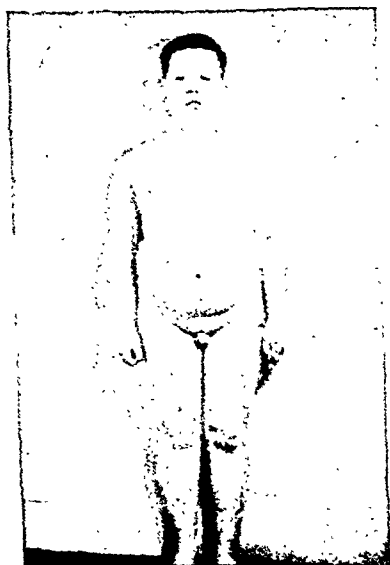


FIG. 1a.—Case of infantile obesity, wrongly diagnosed as Fröhlich's syndrome. Age 11.

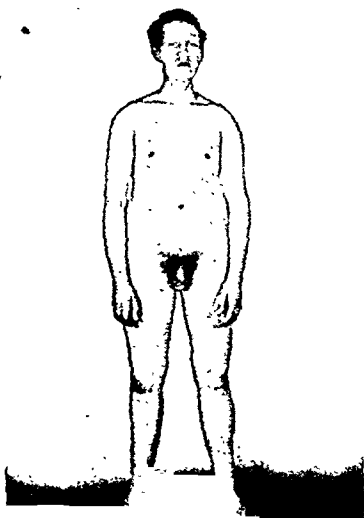


FIG. 1b.—Result of treatment with restricted carbohydrate. No endocrine treatment given. Age 18.

small amounts now available are harmless. Salt should be kept as low as possible and fluid should be limited to 2 pints (1,136 c.cm.) daily, or less in cool weather. The vitamin intake may need supplementing under present conditions. It is found that parents are easily discouraged by over-detailed instructions. The following instructions are unscientific in several respects but they are easy to remember and, if followed conscientiously, invariably effective.

DIET FOR OBESITY

Foods to be avoided:

- (1) Bread and everything else made with flour, except Energen.
- (2) Cereals, including breakfast cereals and milk puddings.
- (3) Potatoes and all other white root vegetables.
- (4) Foods containing much sugar.
- (5) All sweets.
- (6) Salt. If possible no salt should be used in the cooking, other members of the family adding it at table.
- (7) Fluids should be limited to 2 pints (1,136 c.cm.) a day.
- (8) Fats should not be eaten in excess, but the small amount at present available is generally permissible.

Foods that may be eaten without restriction:

- (1) Meat, fish and fowl.
- (2) All green vegetables.
- (3) Eggs, dried or fresh.
- (4) Cheese.
- (5) Fruit, if unsweetened or sweetened with saccharin.

The child should be weighed once a week at the chemist, using the same chemist and wearing the same clothes. On this diet he should lose between half a pound to a pound a week. If he loses more than a pound, you are being unnecessarily strict. If he loses less than half a pound you are not being strict enough.

Thyroid.—It has been pointed out that thyroid deficiency is not a cause of obesity proper, but when there is hypothalamic damage there may be an associated hypothyroidism which needs correction. Moreover, thyroid is an excellent diuretic. It should be used, if at all, only in small doses and with great caution.

Diuretics.—The most satisfactory drug is urea, which can be given without risk for an indefinite time. The dose is 1 teaspoonful three times a day, dissolved in a little fruit squash.

SUMMARY

By way of summary, it may be useful to stress the following points:—

- (1) Obesity in children may occur from overeating and inactivity. In most such cases, in both boys and girls, the distribution of the fat is "Fröhlich-like", "feminine", or "eunuchoid", because of an absence of testicular secretion.
- (2) Analogy strongly suggests that in many patients a hypothalamic lesion exists, although it is usually impossible to describe a specific cause.
- (3) There is no reason to believe that any endocrine gland, except perhaps the posterior pituitary, is abnormal in function. In particular, there

The classical case of *Fröhlich's syndrome* is the best known example. It has been so dangerous a stumbling block for fifty years that it must now be removed from the path of understanding. The original articles have been studied, and the case described again, by Bruch (1939c).

The patient was born in 1887, and was first examined at the age of twelve when he complained of headache and vomiting. There were no physical signs, he was not unduly fat, and his sexual development was normal. A diagnosis of migraine was made. Not long afterwards he began to grow unduly fat. He was seen again at the age of fourteen, when the sight of the left eye was deteriorating and the other symptoms were increasing. The left eye later became completely blind and the right eye began to deteriorate. The excessive fat was laid down chiefly on the abdomen and breasts. At this time the penis was of normal size, the testicles somewhat small, and a few pubic hairs were present. A wrong diagnosis of myxoedema was made and he was treated with thyroid. Concurrently there was an improvement in his eyesight (perhaps because the tumour now found room to expand into the sphenoidal sinus), but when he was eighteen he began to get worse again. At twenty there had been no further sexual development, his general appearance was immature and feminine, he had left optic atrophy and atrophy also of the temporal half of his right disc. A diagnosis of pituitary tumour was then made and operation performed. There was considerable improvement in his vision and the headaches ceased. Erections began a year later, together with an increase in body hair. Biedl examined him in 1913, when he was twenty-six and in the same condition as before. Fröhlich considered that his obesity, the only sign which seemed at all mysterious, was the direct result of his pituitary tumour, but even at that time his explanation was not accepted, Erdheim (correctly, as we now believe) ascribing the adiposity to upward pressure by the tumour on the hypothalamus.

It will be seen then that Fröhlich's syndrome consists of obesity and hypogonadism due to an intracranial tumour affecting the hypothalamus. It is extremely rare. I see two or three cases every week to which this label has been attached, but I have never seen a true case of Fröhlich's syndrome. The explanation is not far to seek. The distribution of fat so often called "the Fröhlich distribution" is the distribution commonly seen when obesity occurs in patients who are not producing testosterone (fig. 1a and b). It is not really a "feminine" distribution but an "unmasculine" one. It is seen also in that obscure but probably hypothalamic genetic disorder, the Laurence-Moon-Biedl syndrome (fig. 2); in the adiposity which follows hypothalamic damage due to encephalitis or severe concussion; and occasionally in adult eunuchs. The "typical eunuchoid" obesity is seen in those eunuchs who happen to become fat; most of them do not.

TREATMENT

The treatment of the fat child differs in no way from that of the fat adult. There are two points of view to be kept simultaneously in mind. The patient is suffering from both fat retention and water retention.

Diet.—Simple reduction in food intake may be sufficient, but in severe cases it is best to prescribe a diet low in carbohydrate and as high in protein as present circumstances allow. Fat need not be completely excluded. To do so makes the diet unpalatable and does not improve the results. The

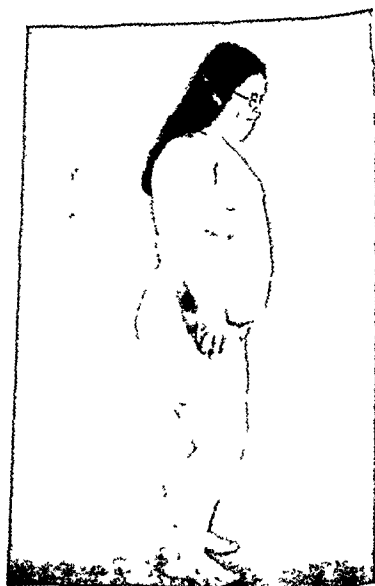
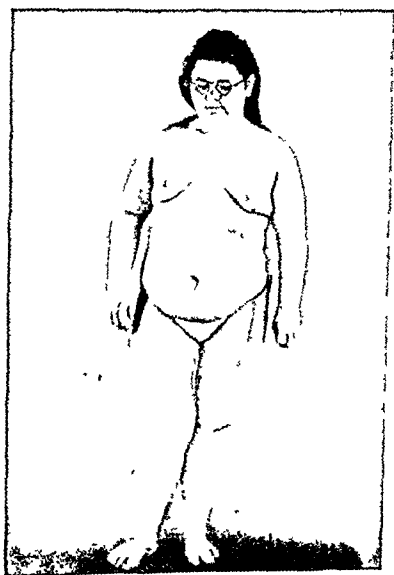
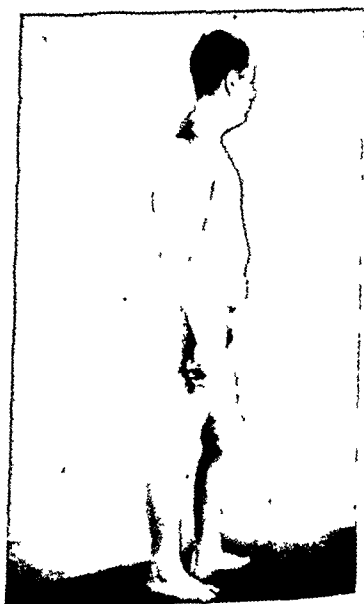
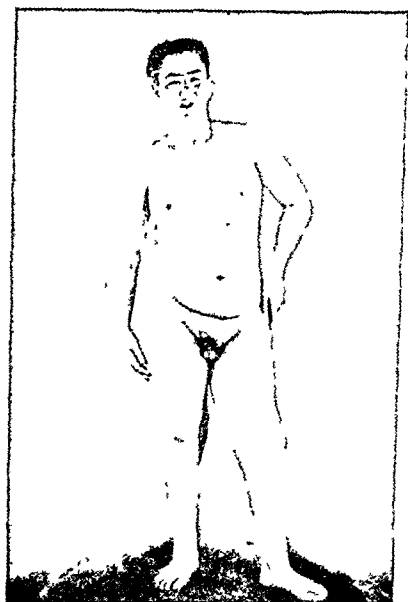


FIG. 2.—Laurence-Moon-Biedl syndrome in brother and sister Ages 16 and 12.

no evidence that the anterior pituitary is concerned. The only possible exception to this statement is afforded by Cushing's syndrome, which is a *hyperpituitary* condition. Treatment by pituitary extract is therefore irrational. It is moreover useless, because pituitary extracts have no potency when given by mouth, and because no commercial extract is effective even when given by injection. There is also no evidence of thyroid deficiency in such cases. Thyroid extract has sometimes a small part in early treatment because of its dehydrating effect. Apart from this, it helps to reduce weight only when given in such dangerous doses as to cause a temporary thyrotoxicosis, which has been known to become permanent.

(4) Water retention is an important factor in most, if not all, cases of adiposity. Anxiety is a common cause of water retention in adults and may be a contributory factor in children.

(5) The majority of fat children grow into normal adults. Despite this they should be treated, for they may otherwise develop feelings of inferiority due to the laughter of their contemporaries and to their inability to shine at games.

(6) The only treatment required for the obesity is a low carbohydrate diet, exercise and diuresis. In those cases in which the hypothalamic lesion has caused a concomitant hypogonadism there is a place for treatment with chorionic gonadotrophin, oestrogens or androgens, in addition to the general measures. Such cases are relatively uncommon.

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In the *artificially fed baby* motions may become formed and hard. The dry crumbling stool suggests too much protein and the milk mixture may need greater dilution with extra carbohydrate. Hard motions may be improved by extra sugar in the feeds, and liquid paraffin or milk of magnesia, $\frac{1}{2}$ to 1 teaspoonful daily, is harmless and a useful addition. They should be given each day, and not only after a hard motion is passed. There are objections to the liquid paraffin preparations, namely, that they prevent absorption of vitamin D and that aspiration of oily particles may lead to pneumonia. Any general practitioner will confirm that these are essentially theoretical and not practical contraindications. Simple medicinal measures of this kind are more satisfactory than the popular prune pulp, which in any event acts more by increasing the bulk of the stool than by any inherent laxative properties.

A cause of infrequent motions in small babies and toddlers is an anal fissure. The child screams and cries when a motion is passed, and the stool may be streaked with bright blood. The child becomes so frightened of the pain that he will refuse to perform. Motions must be kept soft by simple lubricants, and an anæsthetic ointment, such as nestocyl or nupercaine, applied to the fissure may give relief. Insertion of a finger or suppository will only increase the fissure by stretching.

Training plays a big part in teaching a child regular bowel habits. A baby should be "potted" after feeds from a week old, and when older should be encouraged to use the chamber after meals, especially breakfast. This task of the mother or nurse should be done with discretion. Many mothers have become so obsessed with the need for a daily action that a baby is held out for so long that the mother complains she is exhausted, with the baby expressing his views in his own way! Too much potting and making a fetish of the daily ritual leads to a negativistic attitude on the part of the child, who will refuse to have his bowels open, and the more he is cajoled the worse he gets, even to the extent of abdominal distension and pain. Bowel action is a normal function that calls for no undue emotional display if successful or otherwise.

In infants and toddlers it is important to give to constipation the significance it deserves. A constipated baby may be slow in gaining weight, due to poor absorption of his food. This does not call for purgation but for a revision of the diet, correction of anæmia, and an improvement in the general muscle tone. An early cretin must not be missed; these babies are often brought to the doctor for severe constipation, which in their case is only relieved by thyroid therapy. In the toddler, constipation sometimes induces a prolapse of the rectum, although it should be stressed that diarrhoea is a far more common cause of this. Herniæ are often attributed to constipation but are due much more to lack of muscle tone, as is, indeed, the constipation itself.

CONSTIPATION IN CHILDHOOD

By A. G. WATKINS, M.D., F.R.C.P.

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No clinical condition has been more influenced by lay superstition and subtle advertising propaganda than has constipation. Medical men have not been free from a charge of careless thinking in this respect. Not so long ago any and every ailment was promptly treated by a purge and daily dose, whether it was the brimstone and treacle of Dotheboy's Hall or the syrup of figs of the modern nursery. The Saturday night purge is still too popular.

There was some attempt to study the problem in the early part of this century, but the Arbuthnot Lane theories soon became an easy prey for commercial exploitation. In more recent times physicians have come to look upon constipation in its proper perspective. They have realized, for instance, that each and all of us may not have a similar pattern for our bowel action. It is now appreciated that a loaded colon with no evacuation for some few days does not necessarily produce intestinal toxæmia with all its supposed sequelæ. It is often of some comfort to a harassed mother of a child who has had no bowel action for a week to remind her of the gentleman quoted in Samson Wright's "Applied Physiology", who went from June of one year to June of the next, unrelieved but undistressed.

In the consideration of constipation in children it is necessary, as always, to take note of the age of the child; and the problems in infancy and older children are not the same. Moreover, it must be borne in mind that constipation, as the term is used by the mother, may imply either infrequent motions or hard motions that are difficult to pass. Constipation due to intestinal obstruction must receive urgent attention, but this article is not concerned with that aspect of the problem.

CONSTIPATION IN INFANCY AND TODDLERS

Many successfully *breast-fed babies* have infrequent motions, that is to say, they go four to five days or even a week without an action. When a motion is passed, it is normal. During that time the baby is perfectly fit and well—it is the mother who is alarmed and a prey to all sorts of suggestions for treatment to allay the mythical risks of convulsions, and so forth. So long as the baby is contented, is not being sick, and there is no measure of abdominal distension, nothing need or should be done. Suppositories, soap sticks and enemas should be taboo. Reassurance, patience, and small daily doses of milk of magnesia are all that is required.

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CONSTIPATION IN OLDER CHILDREN

The habits of infancy may be carried on. Negativism may persist, so may lackadaisical habits, and the early morning stampede to school may disturb the routine evacuation. Parents and teachers should see that the child has time for an unhurried visit to the lavatory; the bowel will not be fully emptied if time is short.

Diet.—In the older child, diet has more effect on the character of the motions, but there has been perhaps too much swing in favour of dietetic treatment for constipation, which promotes a good deal of fadism. Shortage of fluid is one of the chief causes of hard motions. Excess fruit and roughage will increase the bulk of the motion but they do not necessarily relieve constipation; in fact, too much roughage may induce it. The present-day bread flour and our excessive carbohydrate diet increase roughage and so cause a larger residual colonic content which stimulates a bowel action. It is therefore important to review the type of constipation and diet before giving advice.

Exercise is important in producing a daily action. The pale, flabby, sit-at-home child tends to have infrequent motions, and attention should be paid to the improvement of muscle tone, especially that of the abdominal wall. Such general measures as increased exercise, massage, and a holiday by the sea will improve muscle tone, and removal of septic foci of tonsils and sinuses, correction of anæmia, and the like, are obviously important.

Aperients.—In the child who remains constipated in spite of correct training, diet, and tonic measures, medicinal means may justifiably be used. These must, however, be used regularly and persistently until a normal rhythm is re-established. The pernicious habit of an occasional dose must be avoided. In the mild case simple lubricants of the paraffin type with added agar may be used. The addition of phenolphthalein is valuable as in many of the proprietary preparations, e.g. petrolagar or agarol. The dose must be that required, which can only be determined by trial and error, beginning in the majority of cases with $\frac{1}{2}$ to 1 teaspoonful, once or twice a day. Should these prove unsatisfactory (an unusual event) more potent drugs may be needed, e.g. aloes, sodium sulphate, cascara or one of the vegetable laxatives. A valuable, "old-timer" prescription is as follows:—

R Tincture of aloes	3 minims (0.18 c.cm.)
Sodium sulphate	5 grains (0.32 gm.)
Tincture of belladonna	5 minims (0.3 c.cm.)
Tincture of ginger	5 minims (0.3 c.cm.)
Syrup of peppermint	to 60 minims (3.6 c.cm.)

The aloes may be replaced by syrup of senna, and the mixture may be given once or three times daily, as required. Once the optimum dosage has been determined the medicine should be continued for a week or so; in many cases this will restore the daily habit and the mixture can then be

dropped. Rhubarb and soda has been a valuable and time-honoured remedy, especially if there is mucus in the stools with any suggestion of "liverishness", as shown by pale stools. Such a mixture is:—

R Rhubarb, in powder.....	2 grains (0.128 gm.)
Sodium bicarbonate	2 grains (0.128 gm.)
Tincture of belladonna	5 minims (0.3 c.cm.)
Chloroform water.....	to 60 minims (3.6 c.cm.)

This is best taken before meals, and the above dosage is suitable for a child of five years old. Castor oil should never be given; after its initial purging action it constipates, and there is always the risk of perforating an inflamed appendix.

Enemas and suppositories should be avoided. They cause considerable physical and mental distress, and whereas they may clear the bowel they do not relieve the cause; in fact, by anal stimulation they create the wrong conditioned reflex. A word may be added here on the evil practice, fortunately dying out, of purging and washing out the bowel before an operation; this is a dangerous and needless procedure.

Only the child with simple constipation has been discussed, but in all cases it is obviously important to exclude organic causes. The acute obstruction is usually self-evident, associated as it is with a short history, vomiting, and abdominal distension. The chronic and long-standing constipation of Hirschsprung's disease may be most difficult to recognize in its early stages. Abdominal distension, visible peristalsis, palpable faecal masses with an enlarged colon shown in a barium meal or enema, together with a history of long intervals, sometimes weeks, without an action, betray its presence.

SUMMARY

- (1) The evils of constipation in childhood are more imaginary than real. *Per contra*, diarrhoea, especially in infancy, is a dangerous condition.
- (2) Proper training, sufficient exercise and good muscle tone are as important as diet as means of promoting a healthy bowel action.
- (3) Medicinal measures are not very helpful except the simple lubricants. Correction of the cause is more important than purgation.
- (4) Enemas and suppositories should not be used.
- (5) Care must be taken to recognize constipation due to organic causes, namely, obstruction, megacolon, anal fissure, and thyroid deficiency.

SLEEP DISTURBANCES IN CHILDHOOD

BY HARRY BAKWIN, M.D.

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DISTURBANCES of sleep are very common in children as they are in adults. There may be difficulty in falling asleep, restless sleep, early waking, night-mares and night-terrors, sleep-walking (somnambulism), and sleep-talking (somniloquy). Much less common is excessive sleepiness.

INFANCY

Poor sleep during infancy usually results from physical causes, such as hunger, the indigestion due to overfeeding, the pain and discomfort of swallowed air, the pain and itching of ammoniacal dermatitis, and physical illness, particularly otitis media. During the early weeks of life babies often cry because of a soiled napkin but they quickly lose their fastidiousness and do not regain it again until they approach their first birthday. Babies may cry at night because their room is too warm or too cold or because their clothing is uncomfortable.

Treatment is directed towards correction of the etiologic factors. The food intake should be adjusted to suit the needs of the individual child. When wakefulness and crying are due to air sucked in during feeding the baby should be held over the shoulder several times during feeding, as well as afterwards, to allow expulsion of swallowed air, and the size of the nipple hole should be varied. If necessary a small enema may be given.

In most instances *ammoniacal dermatitis* can readily be controlled. Ammonia is not present in the normal urine in appreciable amounts but is elaborated from the urea in urine through the action of an organism found in the stools. This transformation can be inhibited by impregnating the napkins with an antiseptic substance. For this purpose a saturated solution of boracic acid is sometimes effective. More effective is "diapene" (*p*-diisobutyl-cresoxy-ethoxyethyl dimethyl benzyl ammonium chloride monohydrate), recently introduced by Benson and his co-workers (1947).

THE NORMAL SLEEP HABITS OF CHILDREN

Parental complaints about the sleep of infants often result from lack of knowledge of normal sleep rhythms at this age. The following resumé of the sleep habits of infants is based on the data of Gesell and Ilg (1937).

For the first four to eight weeks after birth the baby sleeps practically all the time, except when he is being fed. He usually awakens with a cry which announces that he is hungry and he lapses into sleep when he has had his fill. The sleep of young babies is light and is readily disturbed. The difference between sleep and wakefulness at this early age is not sharply defined.

Somewhere between the age of three and eight weeks the baby begins to take a long nap, once every twenty-four hours, usually at night, and this is the sign that the night feeding can be omitted. At first there is considerable variation as to the time of waking in the morning, but at three or four months it becomes more regular, and most children at this age are content to wait until 6 a.m. for their morning feed. They may waken with a cry and demand food immediately or they may lie in bed and babble for a while. At this time of day they are apt to be very hungry and to suck vigorously. When allowed to take as much food as they like—as in the case of breast-fed babies—a three to four months' old baby may take as much as 10 ounces (280 c.cm.) at this feed. A nap generally follows. A longer nap follows the 10 a.m. feed, usually out of doors, and another shorter one after the 2 p.m. feed.

A great many babies at three or four months are wakeful during the late afternoon. They may play by themselves for a little while but they usually cry and demand to be picked up and played with. Before the age of three months babies generally prefer to lie on their backs when awake, with the head turned to one or the other side. They may find lying on the face uncomfortable and they will cry and fuss because of the discomfort. At the age of six or seven months the baby is interested in what is going on around him. When not asleep he gurgles and tries to manipulate objects. His sleeping time becomes more definite, usually about ten to twelve hours at night, three hours in the morning and one to two hours in the afternoon. There are often short intervals of sleep during the day lasting for only five or ten minutes, and the baby who was fussy and irritable before, awakes alert and refreshed. Young babies sleep well out of doors and seem to enjoy the rhythmic motion of the perambulator.

The baby can now turn over and adjust his position with ease. He often sleeps with his knees drawn up under him. This is a common position for the infant when put to sleep on his abdomen. Soon after the age of seven months most babies are able to sit up, at first with support, later alone; and then, a little later, they are able to pull themselves up to the sitting position. When this takes place the baby is less willing to sleep in his pram. He wants to look about. It is often necessary to plan time for sleeping in his crib. The sleeping periods become longer and sleep is quieter. Extraneous sounds no longer disturb him as much as before.

During the second year of life sleep is modified in several ways. Going to sleep is now a more or less conscious matter, and sleep no longer comes immediately after being put to bed. Some babies cry, others talk or play or crawl about the crib. About the end of the first year the baby may refuse his morning nap, but then he is generally sleepy during lunch and falls asleep promptly afterwards. When he does sleep in the morning he may refuse a second nap and be so cross and tired by supper time that he cannot eat. This is a good indication that he is ready for one nap a day. The most convenient time is usually after the midday meal. Some babies fall asleep

standing up and then half waken and lie down. At this age, they crawl all over the bed, get out of the covers and sleep in most peculiar positions. Many object to the restraint of tight bed clothes and cry lustily unless allowed to move about. There is great variation in the number of hours different infants will sleep. Each child has his own sleeping rhythm and a schedule should be worked out to suit the individual child.

CHILDHOOD

Faulty training.—In young children the most common cause of sleep disturbance is faulty training. The symptom is rarely an isolated one and usually accompanies other difficulties, particularly poor appetite. Any error in child-rearing which leads to emotional discomfort may manifest itself in this way. The over-indulged child who is accustomed to having his way with his parents may insist on an elaborate ritual at bedtime. He may demand that a parent lie down with him until he is asleep, that he be read to, sung to, rocked. Going to sleep is used as an attention-getting mechanism. The problem is primarily one of discipline and only secondarily of sleeping.

Poor sleep may result from failure to live up to parental expectations at home or in school, from concern over parental rejection or indifference, from resentment against parental over-authority. If there have been difficulties and misunderstandings during the day the child may lie awake to ponder over his problems and to plot revenge for assumed or real injustices; or he may feel guilty about the propriety of his conduct. A child should not be put to bed as a punishment.

Over-stimulation.—Children who are over-active and excitable often find difficulty in falling asleep. In such instances sleep, when it comes, is likely to be restless and accompanied by jerking movements and sleep-talking. Over-excitement may result from too many extracurricular activities, exciting school activities, reading exciting stories, listening to hair-raising radio programmes, or active play immediately before going to bed.

Anxiety and worry are potent causes of wakefulness in older children. There may be concern about unsatisfactory conditions in the home, such as parental incompatibility, parental preference for other siblings, economic difficulty. Frequently worry centres around the school situation. The child may not be doing as good work as he would like to, or his grades may not be as good as he believes he deserves, or he may be concerned about the impression he has made on a favourite or feared teacher. The child may also be concerned about his popularity with schoolmates. During adolescence girls worry about their popularity with men, boys about their athletic prowess and uncertainty about sex.

Fear may keep a child from falling asleep and may make sleep restless. Children who have been over-protected and have not been trained to assume responsibility may be afraid to be alone at night because they have not been accustomed to be alone during the day. In the darkness free play is given to the imagination. The sounds of rattling windows and creaky beds are

endowed with sinister meanings. The child's fearfulness may be further stimulated by reading or listening to horror stories over the radio.

Secret practice of a habit.—Some children remain awake at night in order to practice, in secret, habits which are not permitted during the day, such as nail-biting, thumb-sucking and masturbation.

Curiosity.—Children may lie awake to listen to adult conversation in an adjoining room. If a child shares a room with his parents or sleeps nearby and has had an opportunity to observe the sexual act he may remain awake in order to see more or to ponder what he has already observed.

Suggestion.—Wakefulness in a child may unwittingly be suggested by adults. Casual remarks regarding one's ability to fall asleep or what a poor night one has had may appeal to the child as an attractive adult attitude and he may strive to remain awake in imitation.

MANAGEMENT

A sleep routine should be established early in life and this should be varied as the child's developmental status changes. Sleep routines should be closely adhered to. Going to bed should not be a subject for discussion or argument. The atmosphere preceding bedtime should be leisurely and calm. The child's needs are attended to, he is properly tucked in, given friendly, affectionate reassurance and left alone.

The best guide to the adequacy of sleep is the child's appearance of alertness during his waking hours and the absence of evidence of fatigue.

History taking in a child with a sleeping difficulty should include information about (1) the sleeping arrangements, i.e., whether the child sleeps alone, whether he sleeps in his own room, the presence of disturbing influences in adjoining rooms, the temperature of the room; (2) parental attitudes towards the sleeping situation, i.e., whether the parents are greatly concerned about the child's sleep, with the result that the child uses going to bed as an attention-getting mechanism or as a method of resisting or annoying his parents; (3) the general attitude towards child-rearing which prevails in the home, i.e., whether there are any gross errors in parental attitudes or interparental conflicts; (4) possible interference from a nurse, grandparents or other relatives, and suggested sleep difficulties.

In young children sleep difficulties are generally due to faulty training. In such instances the only regimen which works is to let the child cry it out. A cure can be assured in three nights, sometimes in two. I see no objection to a child's taking a favourite toy or pillow to bed with him. If the child climbs out of bed and comes in to his parent's room he is led back to his own room gently and calmly. This is repeated until the child tires. If he sees that his parents will not yield he will quickly cease these antics. Hypnotics are of no value in this type of sleep disturbance. Occasionally a child will fall asleep readily but will awaken during the night at a certain hour and cry. If no reason can be found for the crying, $\frac{1}{4}$ grain (16 mgm.) of phenobarbitone, for four or five nights, will generally break the cycle.

Complaints about sleep are less common during the school years than earlier. Children should have a regular time for going to sleep and this should not be varied except for definite reasons. The period before bedtime should be quiet and peaceful, without too active play. Poor sleepers should not be allowed to listen to exciting radio stories before bedtime. The factors leading to poor sleep should be explored and corrected.

NIGHTMARES, NIGHT-TERRORS AND SLEEP-WALKING

Nightmares and night-terrors are fright reactions occurring during sleep. In the *nightmare* the child awakens in terror from a dream usually characterized by suffocation and helplessness. He can ordinarily relate his dream, he is well oriented, he recognizes people about him and he can be calmed readily. Sometimes the dream is recalled during the day and the recollection is accompanied by a sense of dread. Nightmares generally take place within an hour or two after going to bed and are not uncommon.

Night-terrors are rare. The child is usually found sitting up in bed or standing or running about, greatly agitated and screaming. He is not fully awake and there are hallucinations of strange persons or animals in the room. The child is disoriented and does not recognize familiar persons about him. He quiets down after a few moments and goes back to sleep without remembering the episode. It may be necessary to waken the child to terminate the attack. Night-terrors may be repeated several times a month with restless nights in the interim; sometimes they subside after a single episode or recur only at long intervals. Nightmares and night-terrors occur in children who are emotionally disturbed and anxious. Treatment must be directed toward the correction of the child's emotional relationships.

Sleep-walking is uncommon before adolescence. In the young child it is usually directed toward the parent's room and may be an attempt to satisfy curiosity about the sexual act or a desire to share the mother's bed. It is possible that the child is seeking in fantasy what he cannot achieve in reality. As with adult somnambulists, some children do constructive things, others do things which are destructive and foolish. Excellent mental and muscular correlation enables them to walk fearlessly upon precarious ledges. The episodes usually end happily but there have been numerous deaths of sleep-walkers. To waken a somnambulist when he is in a dangerous position is inadvisable as it may upset the coordination between mental and muscular activity. The child is usually unaware that he has been out of his bed, even when wakened during his walking, and cannot describe what has happened. Some sleep-walkers speak with great facility and can carry on a conversation.

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THE "RUNNING NOSE"

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PERSISTENT nasal discharge is a condition often encountered in young children. The successful treatment of this condition can sometimes present quite a problem.

THE STRUCTURES INVOLVED

There is the pharynx, with the tonsils; the nasopharynx, the site of adenoids, and throughout this region the mucous membrane is richly studded with lymphoid tissue; the nasal fossæ, with the turbinate bones, and the ostia of the paranasal sinuses which drain into the nose; for it must be remembered that the maxillary sinus and some of the ethmoidal cells are present at birth, although not fully developed. It is usual to divide the nose into three regions—the vestibule, the nasal fossæ, and the paranasal sinuses.

The vestibule is that part of the nasal passage enclosed by the lower cartilaginous framework of the nose. It extends from the anterior nares to the atrium meatus nasi, and is lined by stratified flat epithelium. Where the lining is continuous with the surrounding skin there are superficial horny cells. There are also vibrissæ, sebaceous and sudoriferous glands. This layer gradually merges into the Schneiderian membrane, and sero-mucous glands replace the sudoriferous glands.

In *the nasal fossa* proper there is a ciliated cylindrical type of epithelium containing many glands. In certain areas, particularly at the anterior and posterior ends of the inferior turbinal, this layer is of considerable thickness due to cavernous tissue in the tunica propria, where there is a capillary network beneath the epithelium and surrounding the glands. This capillary network is encircled by circular and longitudinal unstriated muscle bundles which give it the character of erectile tissue. There is a reflex nerve control of this erectile tissue which is of the utmost importance to the proper functioning of the nose. The mucous and serous glands provide the protective fluid covering for the lining.

The paranasal sinuses, as already stated, drain into the nose; their lining mucous membrane is continuous with that of the nasal fossæ, differing only in that there are fewer glands and no erectile tissue.

THE FUNCTIONS OF THE NOSE

The main functions are respiratory and olfactory. The upper third of the fossæ is the olfactory area and does not require further mention. The respiratory function consists of filtering, heating and moistening the inspired air, and it is essential for a healthy nose that this physiological function is not interfered with in any way. Lack of moisture, the application of many

drugs and heavy oils, will arrest the ciliary motion and cause stagnation. Obstruction to the air-stream will have a similar effect. In such circumstances, infecting organisms can gain entrance to the mucous membrane.

THE CAUSES OF NASAL DISCHARGE

The character of the discharge may vary from that of a clear watery nature to mucoïd, muco-purulent or purulent; it may at times be blood-stained.

In the infant the presence of a unilateral or bilateral choanal atresia should be ascertained. This can be accomplished by passing a fine probe along the inferior meatus while palpating the nasopharynx. If this examination is not carried out a unilateral atresia may certainly be overlooked, as the child may be breathing through the unaffected nostril and keeping the mouth closed. In the case of a bilateral atresia the child is obviously unable to breathe through the nose; the mouth is open and respiration is laboured, as the tongue often tends to fall back. There is also great difficulty in sucking. In such a condition the nose is often full of crusts coating the walls. This, together with lack of an air-stream, results in a superadded infection and discharge. These cases present great difficulties in treatment, as the obstruction may be due to a bony or a membranous diaphragm. The maintenance of an opening following perforation of the diaphragm is the main problem; continuous dilatation is necessary and may lead to changes in the mucous membrane of the nose. Fortunately, this condition is rare and is usually unilateral.

In the first three months of life inherited syphilis may manifest its presence in the form of "snuffles". It is characterized by an obstinate nasal discharge which tends to dry up and form crusts. The irritation caused by the discharge may lead to the appearance of fissures at the anterior nares. In infants so affected other evidence of the disease, together with the family history, should be investigated. If this diagnosis is established, specific treatment should be instituted.

An infant may have recurring attacks of nasal discharge, possibly due to dietetic errors and lack of proper ventilation of the nose, through lack of exposure to fresh air by day and night. If the home conditions of some of these infants are inquired into it is often found that they are living in an overcrowded, over-heated room with very inadequate ventilation. In these cases the discharge does not show much tendency to crust, but may produce considerable irritation of the anterior nares and the upper lip. After gently cleansing the nostrils the instillation of a few drops of 10 per cent. argyrol has been found to be of value.

An infant who has had several bouts of nasal discharge may have developed quite a pad of infected adenoids, and if this fact is determined by palpation of the nasopharynx the adenoids should be removed.

CAUSAL FACTORS IN THE OLDER CHILD

Foreign bodies.—In older children, of an age when they can toddle or walk

about, a favourite pastime appears to be the pushing of all manner of objects into their noses. These objects range from pieces of paper to beads, peas, and cherry stones. Unless they have been detected in the act the presence of the foreign body remains unsuspected until a nasal discharge is noticed. This discharge is persistent and gradually becomes purulent. If the object is one which will swell with moisture there may be some swelling and obstruction of the nose. In any child with a purulent unilateral discharge the presence of a foreign body should at once be suspected.

On examination, after cleansing the nostril, the foreign body may be seen and can be removed with a pair of toothed forceps. A fine probe with about a quarter of an inch of its tip bent to a right angle has been found most useful for this purpose. It is passed beyond the object and then withdrawn. Should the foreign body have been lodged in the nostril for a considerable period there will be a reactionary swelling of the mucosa and some ulceration, resulting in the body's becoming embedded. In such circumstances the application of pledgets of wool squeezed out in 5 per cent. cocaine solution with an equal part of adrenaline will shrink the mucosa and render removal much easier. When dealing with very young children it is often better to administer a general anæsthetic.

Following removal of the foreign body no further treatment is required, as the discharge usually clears up.

Diphtheria.—The presence of blood streaks in a nasal discharge should suggest the possibility of diphtheria, and swabs should be taken and a virulence test carried out. In these cases membrane may be seen in the nostril; the discharge is usually clear at first, but in a day or two becomes sanguinous or purulent. Further, there may be attacks of epistaxis. Anterior nasal diphtheria is the mildest form of the disease; its significance rests on its potentiality for spreading the infection to others.

Tonsils and adenoids.—Following scarlet fever and measles there is often a residual muco-purulent or purulent discharge. The tonsils and adenoids in such cases are infected, whilst in older children the antra and ethmoids may be involved. Children of about school age should be examined for diseased tonsils and adenoids, and if present, operation should be advised. A persistent watery discharge is often associated with adenoids.

From this age onwards, if there is a persistent nasal discharge, alike in those children with or without tonsils and adenoids, a possible infection of the paranasal sinuses should be kept in mind. Skiagrams of the sinuses will furnish evidence, especially if the condition be unilateral, when a comparison of the two sides can be made. Children show an apparent thickening of the mucous membrane lining one or both antra. This may be due to a chronic infection, but on the other hand the lining membrane in the sinuses is likely to be thicker in children than in adults, as the developing sinus has a more active lining. The thickening may also be due to an allergic condition, and in this event there may be associated œdema with swelling of the inferior turbinals and a thin watery discharge.

It is outside the scope of this article to make more than a reference to allergy, vasomotor rhinitis, and hay fever. These conditions are met with in children and entail a long, careful, and often fruitless search for the causative

factor. The nasal obstruction usually present may be relieved by ephedrine sprays. By mouth, ephedrine and, more recently, benadryl have been of value. The indiscriminate use of the cautery should be avoided. Puncture cautery of the œdematous inferior turbinals is preferable, as this entails less destruction of the surface epithelium.

True hypertrophic rhinitis may also be met with, giving rise to some discharge and obstruction. This condition generally involves the inferior turbinal, the anterior or posterior ends, or there may be a fringe-like enlargement extending along the length of the turbinal. On posterior rhinoscopy the posterior end shows a typical mulberry-like swelling in the posterior choana. True hypertrophic rhinitis is diagnosed only after the application of 5 to 10 per cent. cocaine solution. Vascular engorgement will subside, whereas true thickening will remain. Operative interference should be as conservative as possible. Formerly life was made a misery for many patients by far too wide and indiscriminate removal of turbinals. The nose was reduced to a dry and crusted cavity, often accompanied by fœtor.

If the skiagrams suggest the presence of pus by the appearance of a fluid level the antrum should be washed out by puncturing through the inferior meatus. In young children this may safely be carried out under a general anæsthetic by using a fine cannula fitting on to a Record syringe. This is passed through the puncturing needle and a few c.cm. of saline are injected into the antrum and then sucked out again. The fluid obtained can be examined for organisms. Two or three washings will generally clear up a recent infection.

Chronic infection will require an intranasal antrostomy. The radical Caldwell-Luc operation should not be lightly undertaken in young children, as interference with the permanent teeth may result.

Deviations of the nasal septum must also be mentioned. In children this usually involves the columellar cartilage, which may be dislocated to one or other side, resulting in a varying amount of obstruction. Unless this obstruction is acute it is better not to interfere, as the future development of the nose may be affected.

THE DIETETIC FACTOR

Diet surely plays an important part, and many children receive far too great an amount of carbohydrate and not nearly enough in the way of fats. Lack of vitamins also plays a part, especially A and D. These children should get as much fresh air and sunshine as possible, and should sleep in well-ventilated bedrooms; conditions not easy to fulfil at the present time. These dietetic defects, lack of vitamins and fresh air, would appear to bring about a type of generalized catarrh of the mucous membranes. Further, nasal breathing exercises and correct posture should be practised; the former are of the utmost importance following removal of adenoids.

Conclusion.—Emphasis is placed on the importance of the nasal mucous membrane, with the object of pleading for it to be treated with great respect. Do not prescribe douches or sprays that contain drugs or bases which will paralyse the cilia and impair the correct functioning of the nasal lining, and do be conservative in operating.

THE DIET FOR THE SICK CHILD

BY FLORENCE DILLISTONE, S.R.N.

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THE majority of sick children dislike being fussed and worried over food; arouse their interest in the subject and the first objective is gained. A friendly, matter-of-fact chat will win the child's confidence and at the same time furnish a useful amount of information relative to food habits and idiosyncrasies. It is a good policy to maintain a daily personal contact with the child and to submit to him a choice of dishes; this will establish in his mind a feeling of self-importance and a desire to cooperate. The attitude of the difficult child will change from boredom and disinterest to anticipation and enjoyment of his diet.

DIET FOR THE TREATMENT OF CÆLIAC DISEASE

The diet is arranged in four stages (table 1). Stage one is a preliminary period of rest to the gastro-intestinal tract and covers a period of four to six days. Stage two follows, the duration of which is usually a further period of six days. After ten to twelve days of rest the stools are less frequent and more formed, abdominal distension is less, and appetite returns. During this period there is no marked loss in weight; it remains at a constant level during the last six days of the rest period. Stage three is now begun and usually occupies from six to nine months. The calories may be increased by giving larger helpings of the foods allowed. Stage four is gradually introduced until it is entirely established and is continued for a period of six months. After this the child may be given a normal diet with restricted starch.

The whole of the dietary regime has a high protein content with moderate amounts of fat; the important feature is the choice of carbohydrates, which are selected from the non-starch-containing foods in the first three stages. Soya bean flour, in which the carbohydrate is present in the form of achroo-dextrin, is used for cooked preparations. Fruits and vegetables are selected from a low-starch-containing group. Starch is introduced into stage four in small amounts; this may be increased for children who are able to hydrolyse and absorb starch. Dextri-maltose is the sugar of choice, as sucrose is not well tolerated during the early stages of the disease. Vitamin supplements are given throughout the treatment.

DIET FOR INFANTS WITH FIBROCYSTIC DISEASE OF THE PANCREAS

Use is made of peptonized skimmed milk of a proprietary preparation of predigested casein (Peptalac) with added protein hydrolysate. The carbohydrate is given in the form of predigested wheat flour (Benger's or Savory

TABLE I
DIET SHEET FOR CHILDREN WITH COELIAC DISEASE

						Carbohydrate gm	Protein gm	Fat gm
6 a m	8 oz (227 c cm) Prosol	1	in	8	8 0	17 4	
	20 gms dextri-maltose	20 0		
10 a m.	7 oz (198 6 c cm) Beurlac	13 2	8 1	2 5
	20 gm. dextri-maltose	20 0		
2 p m	8 oz (227 c cm) Prosol	8 0	17 4	
	20 gm dextri-maltose	20 0		
6 p m	7 oz (198 6 c cm) Beurlac	13 2	8 1	2 5
	20 gm dextri-maltose	20 0		
10 p m	8 oz (227 c cm) Prosol	8 0	17 4	
	20 gm dextri-maltose	20 0		
						150 4	68 4	5 0

Calones 920

STAGE II

						Carbohydrate gm	Protein gm	Fat gm
6 a m	8 oz (227 c cm) Prosol	8 0	17 4	
	20 gm dextri-maltose	20 0		
10 a m	7 oz (198 6 c cm) Beurlac	13 2	8 1	2 5
	20 gm dextri-maltose	20 0		
	4 oz (120 gm) banana purée	22 0	1 8	
2 p m	8 oz (227 c cm) Prosol	8 0	17 4	
	20 gm dextri-maltose	20 0		
6 p m	7 oz (198 6 c cm) Beurlac	13 2	8 1	2 5
	20 gm dextri-maltose	20 0		
	4 oz (120 gm) banana purée	22 0	1 8	
10 p m	8 oz (227 c cm) Prosol	8 0	17 4	
	20 gm dextri-maltose	20 0		
						194 4	72 0	5 0

Calones 1,110

STAGE III

						Carbohydrate gm	Protein gm	Fat gm
8 a m.	8 oz (227 c cm) Prosol	8 0	17 4	
	20 gm dextri-maltose	20 0		
	4 oz (120 gm) sieved banana (dried or fresh)	22 0	1 8	
	1 oz (30 gm) dextrinized rusk	11 6	0 8	1 2
	1 oz (7 5 gm) butter			6 0
12 noon	1 oz (30 gm) finely minced liver, chicken or beef (very lightly cooked)		5 5	3 0
	2 oz (60 gm) sieved cooked beetroot	5 6	1 0	
	1 oz (30 gm) sieved cooked spinach, cauliflower or sprouts	0 2	0 4	
	4 oz (120 gm) raw sieved tomatoes	3 2	1 2	
	5 oz (150 gm) Yoghurt or 1 oz (15 gm) Cottage cheese	7 0	4 5	5 5
	1 oz (15 gm) honey	10 0		
	4 oz (120 gm) fruit puree	10 0		
4 p m.	8 oz (227 c cm) Prosol	8 0	17 4	
	20 gm dextri-maltose	20 0		
	1 oz (30 gm) soya bean flour biscuits	9 5	4 6	5 9
6 30 p.m	8 oz (227 c cm) Prosol	8 0	17 4	
	20 gm dextri maltose	20 0		
	4 oz (120 gm) banana purée	22 0	1 8	
						185 1	73 8	21 6

Calones 1,190

STAGE IV

		Carbohydrate gm.	Protein gm.	Fat gm.
8 a.m.	8 oz. (227 c.cm.) Prosol	8.0	17.4	
	20 gm. dextrin-maltose	20.0		
	$\frac{1}{2}$ oz. (15 gm.) cornflakes	9.0	3.8	
	$\frac{1}{2}$ oz. (15 gm.) Bemax	5.0	5.0	
	1 oz. (30 gm.) National bread toasted	15.8	2.4	
	$\frac{1}{2}$ oz. (7.5 gm.) butter			6.0
	$\frac{1}{2}$ an egg dried or shell		3.4	3.0
			8.2	4.5
12 noon	1 $\frac{1}{2}$ oz. (45 gm.) minced liver, chicken or beef or lamb			
	1 oz. (30 gm.) mashed potato or			
	2 oz. (60 gm.) cooked beetroot	5.0		
	2 oz. (60 gm.) cooked chopped spinach, cauliflower			
	or sprouts or salad	0.4	0.8	
	4 oz. (120 gm.) sieved tomato	3.2	1.2	
	5 oz. (150 gm.) Yoghurt or 5 oz. (150 gm.) egg			
	custard	7.0	4.5	5.5
	$\frac{1}{2}$ oz. (15 gm.) honey	10.0		
	4 oz. (120 gm.) fresh or dried fruit	10.0		
4 p.m.	8 oz. (227 c.cm.) Prosol	8.0	17.4	
	20 gm. dextrin-maltose	20.0		
	1 oz. (30 gm.) National bread toasted	15.8	2.4	
	$\frac{1}{2}$ oz. (7.5 gm.) butter, marmite, honey or jam			6.0
	1 oz. (30 gm.) soya biscuits	9.5	4.6	5.9
6.30 p.m.	8 oz. (227 c.cm.) Prosol	8.0	17.4	
	20 gm. dextrin-maltose	20.0		
	1 oz. (30 gm.) National bread toasted	15.8	2.4	
	$\frac{1}{2}$ oz. (7.5 gm.) butter			6.0
	$\frac{1}{2}$ oz. (15 gm.) Cottage cheese			
	(5 oz. (152 c.cm.) milk)		4.5	5.5
	Medium sized apple, pear, orange, grapefruit,			
	banana or grapes	10.0		
		200.5	95.4	42.4

Calories 1,565.6

Dietary regime.—Feeds given four-hourly, number of feeds 5. Amount given at each feed 6 to 8 oz. (180 to 240 gm.)

Fruit juices sweetened with honey given between 10 a.m. and 2 p.m. and 2 p.m. and 6 p.m. feeds.

Vitamin preparations.—Benerva Co. 2 tablets daily, or Bemax tablets, 3 daily. Halibut-liver oil, 10 drops daily. Ascorbic acid, 50 mgm., when fresh juices are not available.

Explanatory notes.—Prosol is a high protein food with 1 per cent. fat content (Trufood).

Beurlac is a powdered buttermilk (Cow and Gate).

Yoghurt is an acidophilus milk; acidity 0.8; pH 5.3 (United Dairies).

and Moore's food). Dextrin-maltose is added as a sweetening agent. Pancreatin, 20 grains (1.3 gm.), is given three times daily before meals. The infant is fed to his expected weight plus an excess for loss caused by faulty digestion and vomiting. Vitamins supplement the diet in correct amounts.

The following is a suitable mixture for an infant aged six months whose expected weight is 16 lb. (7.26 kgm.):—

30 oz. (840 c.cm.) of skimmed peptonized milk.

5 oz. (140 c.cm.) of water, 1 oz. (28.4 c.cm.) dextrin-maltose.

15 gm. protein hydrolysate, 2 oz. (57 c.cm.) Benger's or Savory and Moore's Food.

Nutritive value of formula 120 gm. carbohydrate; 49.2 gm. protein; 20 gm. fat. Calories 856. Divide into five feeds each containing seven ounces of the mixture.

Mixed feeding.—Begin with one to two teaspoonsful of sieved or tinned homogenized vegetables before the 2 p.m. feed; if this is well tolerated add a teaspoonful of finely minced liver, making a broth with marmite gravy. This may be followed by a tablespoonful of baked egg custard or yoghurt sweetened with honey and sieved fruit; this meal will replace the 2 p.m. bottle feed. Pounded steamed fish and scraped lean beef may also be added. Soya bean flour may be added to soups; dextrinized rusks and butter may be given when teeth have erupted. Make use of the non-starch-containing

TABLE I
DIET SHEET FOR CHILDREN WITH CÆLIAC DISEASE

						Carbohydrate gm	Protein gm	Fat gm
6 a.m.	8 oz (227 c cm) Prosol	1	in	8	8 0	17 4	
	20 gms dextrin-maltose	20 0		
10 a.m.	7 oz (198 6 c cm) Beurlac	13 2	8 1	2 5
	20 gm dextrin-maltose	20 0		
2 p.m.	8 oz (227 c cm) Prosol	8 0	17 4	
	20 gm dextrin-maltose	20 0		
6 p.m.	7 oz. (198 6 c cm) Beurlac	13 2	8 1	2 5
	20 gm dextrin-maltose	20 0		
10 p.m.	8 oz (227 c cm) Prosol	8 0	17 4	
	20 gm dextrin-maltose	20 0		
						150 4	68 4	5 0

Calories 920

STAGE II

						Carbohydrate gm	Protein gm	Fat gm
6 a.m.	8 oz (227 c cm) Prosol	8 0	17 4	
	20 gm dextrin-maltose	20 0		
10 a.m.	7 oz (198 6 c cm) Beurlac	13 2	8 1	2 5
	20 gm dextrin-maltose	20 0		
	4 oz (120 gm) banana purée	22 0	1 8	
2 p.m.	8 oz (227 c cm) Prosol	8 0	17 4	
	20 gm dextrin-maltose	20 0		
6 p.m.	7 oz (198 6 c cm) Beurlac	13 2	8 1	2 5
	20 gm dextrin-maltose	20 0		
	4 oz (120 gm) banana purée	22 0	1 8	
10 p.m.	8 oz (227 c cm) Prosol	8 0	17 4	
	20 gm dextrin-maltose	20 0		
						194 4	72 0	5 0

Calories 1,110

STAGE III

						Carbohydrate gm	Protein gm	Fat gm
8 a.m.	8 oz (227 c cm) Prosol	8 0	17 4	
	20 gm dextrin maltose	20 0		
	4 oz (120 gm) sieved banana (dried or fresh)	22 0	1 8	
	½ oz (15 gm) dextrinized rusks	11 6	0 8	1 2
	½ oz (7 5 gm) butter			6 0
12 noon	1 oz (30 gm) finely minced liver, chicken or beef (very lightly cooked)		5 5	3 0
	2 oz (60 gm) sieved cooked beetroot	5 6	1 0	
	1 oz (30 gm) sieved cooked spinach, cauliflower or sprouts	0 2	0 4	
	4 oz (120 gm) raw sieved tomatoes	3 2	1 2	
	5 oz (150 gm) Yoghurt or ½ oz (15 gm) Cottage cheese	7 0	4 5	5 5
	½ oz (15 gm) honey	10 0		
	4 oz (120 gm) fruit puree	10 0		
4 p.m.	8 oz (227 c cm) Prosol	8 0	17 4	
	20 gm dextrin-maltose	20 0		
	1 oz (30 gm) soy a bean flour biscuits	9 5	4 6	5 9
6 30 p.m.	8 oz (227 c cm) Prosol	8 0	17 4	
	20 gm dextrin-maltose	20 0		
	4 oz (120 gm) banana purée	22 0	1 8	
						185 1	73 8	21 6

Calories 1,190

As progress continues add some animal protein—chicken, rabbit, white fish, veal, lamb, and liver, with vegetables. Salt should be omitted entirely from cooking. A normal diet may be resumed at the end of six weeks with restriction of salt.

(2) *Chronic nephrosis with œdema and albuminuria.*—In this stage of the disease a diet with a low sodium content has a very definite value. A diet containing 150 to 200 mgm. of sodium will not allow the child to get into a positive sodium balance and there will be a gradual diminution of extra-cellular fluid. Restriction of fluid intake will not be necessary; the child should be given sufficient fluid to satisfy thirst. After the œdema has disappeared a sodium-restricted diet must be continued to prevent recurrence of œdema until there is evidence of improvement in renal function.

Vitamin preparations should be given daily.

The following is a planned daily diet suitable for children between three years and five years of age, to contain 148 mgm. of sodium. The diet is divided into breakfast, luncheon, and a tea-supper meal (table 2).

HIGH PROTEIN DIETS SUITABLE FOR BURNS, FRACTURES AND ŒSOPHAGEAL STRICTURES

To increase the protein content in the diet of small children for whom a high protein intake is desired, use is made of a fortified or enriched cow's milk mixture. When the child is capable of digesting animal protein the use of protein hydrolysate is an unnecessary expense. Use is made of household skimmed milk powder. When this is unobtainable a proprietary brand of separated dried milk powder is used (separated Cow and Gate, or Prosol [Trufood]).

The following (table 3) is a suitable daily formula for children between the ages of two and four years:—

TABLE 3

	Carbohydrate gm.	Protein gm.	Fat gm.
1½ pints (852 c.cm.) of cow's milk	42.0	27.0	33.0
3 oz. (85 gm.) household skimmed milk powder, or separated Cow and Gate..	42.0	29.0	
Calories 857	84.0	56.0	33.0

The milk mixture may be sweetened and flavoured as desired; during the twenty-four hours the child is given four beverages each containing 6 fluid ounces (170 c.cm.), the remaining 6 ounces may be used in the preparation of a sweet for the midday meal.

The above mixture is in addition to the child's ordinary menu for the day. As appetite improves and an average amount of protein is consumed from animal sources, a corresponding reduction is made in the amount of milk mixture given during the twenty-four hours.

foods during the early stages of weaning. Later the starch-containing foods may be introduced gradually until weaning is completed.

DIET FOR THE TREATMENT OF NEPHRITIS

(1) *Acute nephritis with albuminuria and hæmaturia*.—Dietary treatments aim at relieving the renal system of all unnecessary work. Fluid is restricted to 1½ pints (852 c.cm.) in the twenty-four hours; this should include 15 ounces (420 c.cm.) of milk, the remainder may be used as a vehicle for carbohydrate taking, consisting of diluted fruit juices and jelly. In a diet containing 700 calories the milk will contribute 285 calories; the remaining 415 calories should be given in the form of sugar or glucose. With improvement in the child's condition, appetite returns, and the following additions may be made to the diet:—junket, egg custard, milk pudding, fruit, bread and butter, and biscuits.

TABLE 2

	Na. mgm.	Carbo- hydrate gm.	Protein gm.	Fat gm.
1½ pints (852 c.cm.) synthetic milk (McCance and Widdowson)		37.0	30.0	33.0
1 egg (2 oz. [60 gm.])	76.0		6.8	7.0
3 oz. (90 gm.) yeast-made, unsalted bread	5.0	47.0	7.2	0.9
¾ oz. (22.5 gm.) unsalted margarine or butter				18.0
1 oz. (30 gm.) unsalted biscuits (special recipe)	1.0	12.0	1.4	6.5
2 oz. (60 gm.) beef, mutton, chicken or rabbit	50.0		10.0	6.0
2 oz. (60 gm.) cooked potato	2.0	10.0	0.8	
1 oz. (30 gm.) cooked carrot	4.0	1.2		
2 oz. (60 gm.) cooked cabbage, cauli- flower, green peas or spring greens, or lettuce and tomato	6.0			
½ oz. (15 gm.) semolina, macaroni or semolina	2.0	11.0	2.5	
1 oz. (30 gm.) sugar or the equivalent ..		30.0		
4 oz. (120 gm.) of citrus fruit, apple, pear, banana, grapes, peaches or plums	2.0	10.0		
Calories 1,506	148.0	158.2	58.7	71.4

Note: Honey, jam and barley sugar contain low amounts of sodium and may be given as desired. The meat is calculated as raw without bone. The synthetic milk may be flavoured with coffee or black currant purée. The low sodium milk has been devised by McCance and Widdowson to meet the nutritional requirements of this type of diet. Cow's milk contains 50 mgm. of sodium per 100 c.cm. and is unsuitable. Baking powder and baking soda must not be used in cooking. Tinned vegetables contain added salt and should not be used. Ordinary, commercially prepared bread has a high sodium content; yeast-prepared, unsalted bread is used instead.

Low sodium biscuit recipe.—4 oz. (120 gm.) unsalted fat (lard or margarine); 4 oz. (120 gm.) sugar; 6 oz. (180 gm.) national plain flour; one dried egg, water to mix.

diluted and 1 grain (65 mgm.) of sodium citrate added to each ounce (28.4 c.cm.) of whole milk. Drinking straws provide children with a good deal of pleasure and milk beverages are often sucked up through a straw when they are rejected if given to drink in the ordinary way.

To increase the carbohydrate content of the diet any of the proprietary starch-containing foods may be added to milk. Ices provide an excellent vehicle for all food properties. A Neapolitan ice containing 333 calories may be made from a custard, using $\frac{1}{2}$ pint (189 c.cm.) milk, 1 egg, 1 ounce (30 gm.) of sugar; the cooked mixture is suitably flavoured and coloured before freezing. Delicious and nutritious sweets much enjoyed by children can be made from equal parts of dried household milk powder and golden syrup.

The syrup is brought to boiling point and kept at this point until it forms a soft ball when dropped into cold water. The milk powder is then stirred into the syrup and allowed to cool; flavouring and colouring may be added and the mixture is formed into suitable sized sweets.

Savoury soups may be made with milk and sieved vegetables, two or three teaspoonsful of finely grated cheddar cheese may be stirred into the soup before serving. The cheese should not be allowed to cook in the soup.

Jellies, sweetened fruit juice, and prepared raw fruit may be given as desired.

With improvement in the child's condition, appetite returns and gradual additions should be made to the diet from the following foods: minced chicken, rabbit, lamb or liver. Steamed or grilled white fish, eggs, sieved vegetables, cereal puddings and custards, sponge cake, biscuits, thin, crustless bread and butter, jam and honey. When fresh fruit juices are not available *vitamin supplement of ascorbic acid should be given daily.*

DIET FOR THE POSTOPERATIVE TREATMENT OF TONSILLECTOMY

After the removal of enlarged tonsils the swallowing capacity of children differs; many children are only able to swallow with difficulty and others are less affected and are capable of enjoying a substantial type of diet within forty-eight hours of operation.

For the child who finds swallowing painful and difficult, alternate iced fruit drinks, iced milk shakes and soft ice cream are appreciated. The flow of icy fluid over the painful area is soothing, and small amounts should be given at frequent intervals when the child is awake during the first forty-eight hours. After this the child should be encouraged to swallow a diet nearer the normal consistency; he should be given warm broths and soups containing finely minced meat and sieved vegetables, egg custard and creamy milk puddings with sieved fruit and jelly. Quite soon the diet should become more solid, consisting of lightly cooked eggs, breakfast cereals, thin, crustless bread and butter, chopped meat and vegetables, fish and grated cheese. At the end of six days he should be having a normal diet.

DIET IN THE TREATMENT OF INFECTIVE HEPATITIS OR CATARRHAL JAUNDICE

During the initial stage of the disease in children, nausea and vomiting are often present. Fruit juices suitably diluted with water, to which glucose is added, and citrated diluted skimmed milk should be given at frequent intervals. When this stage has passed a diet containing a relatively high amount of casein is given. Casein is a good source of the lipotropic factor—methionine—one of the essential amino-acids. Liver is also a source of another lipotropic factor, choline, and should be included in the diet whenever possible.

The carbohydrate content of the diet should be high and the fat content low. Vitamin B₁ and B₂ complex may be given in one of the proprietary preparations or food yeast, 5 to 10 gm. daily. Food yeast is especially cultivated for oral administration and is more palatable than brewers' or bakers' yeast. The following diet contains 276 gm. carbohydrate, 70 gm. protein, 20 gm. fat, and is suitable for children from three to five years of age.

On waking: The juice of one orange diluted with water and sweetened with sugar.

Breakfast: Four tablespoonsful of breakfast cereal with special milk mixture and sugar.

One slice of toast (no butter). Honey or marmalade.

Weak tea with milk from special mixture.

Mid-morning: Beverage made with special milk mixture, sweetened with sugar.

Luncheon: 1 oz. (30 gm.) lean meat, liver, chicken or rabbit, or 2 oz. (60 gm.) white fish.

2 oz. (60 gm.) cooked potatoes, small helping sieved vegetable.

Cereal pudding or custard, using special milk mixture.

Sieved fruit or black currant purée.

Tea: One slice of toast or 4 rusks (no butter), honey or jam.

Sponge cake or sweet biscuits.

Weak tea with special milk and sugar.

Supper: Fresh fruit salad, jelly, or skimmed milk ice cream.

Sponge cake or rusks.

Beverage made with special milk mixture.

Late evening: Beverage—Ovaltine or Bournvita made with special milk mixture.

Daily allowances: 1½ pints (852 c.cm.) of hand-skimmed milk to which is added 3 oz. (85 gm.) household skimmed milk powder (special milk mixture).

2 oz. (60 gm.) sugar. 1 oz. (30 gm.) honey or jam.

2 oz. (60 gm.) glucose. 1 oz. (30 gm.) boiled sweets.

DIET DURING A FEBRILE ILLNESS (PNEUMONIA, SCARLET FEVER, ENTERIC FEVER AND RHEUMATIC FEVER)

During a prolonged fever there is an increase in metabolism with a corresponding breakdown of endogenous protein which must be replaced from dietary sources. Carbohydrate is required as a protein sparer and also to maintain the glycogen in muscle and liver tissue.

In the early stages of the illness easily assimilated foods should be given in small amounts at frequent intervals. Milk will form the basic constituent of the diet; this may be served in a number of ways to tempt the capricious appetite of the sick child. When milk is not well tolerated it may be suitably

quantities have to be dispensed. The following prescription may, or may not be copied from a proprietary preparation, but it is an example of the kind of thing which sometimes is demanded; it is a copy of an actual prescription received for dispensing on a N.H.I. script:—

Strontii Lact.	4 oz.
Lith. Cit.	2 oz.
Caffein.	3 oz.
Ac. Citric	3 oz.
Sod. Benz.	1 lb. 8 oz.
Acacia Pulv.	1 lb. 8 oz.
Lactose	1 lb. 6 oz.
Amyli	2 lb.
Mag. Sulph. Ex.	3 lb.
Sod. Sulph. Ex.	12 lb. 8 oz.
Quinin. Sulph.	6 oz.

Mitte $\bar{3}$ ii

OVERDOSES

If all doctors would follow the practice of the few who initial all overdoses, much worry and trouble could be avoided. Those drugs and preparations which have a "normal" dose, but which in certain diseases are given in quantities greatly in excess of the normal dose, provide examples. Overdoses of dangerous drugs to which the patient may have become tolerant present a special difficulty; enormous doses of morphine are sometimes necessary to produce the required effect, and again the cooperation of the doctor in indicating that he is aware of the abnormality would be appreciated by the pharmacist. Some of the œstrogenic substances present unusual difficulties, as their maximum doses appear to be undecided, and the chemist is often left to find out whether a large dose, much in excess of the average, is actually intended. Stilbœstrol, for example, is quoted as having a maximum dose of 5 mgm., yet 50 mgm. and 100 mgm. doses are not uncommon.

INSULIN

Insulin is often ordered in a way which does not make clear the intentions of the doctor. Such prescriptions as:—

20 c.c. 80 units

are not infrequent; but no mention of the drug required has been made. Often the number of units and the number of cubic centimetres are transposed, or a number of units which could not possibly be dispensed may be ordered. The ideal method of ordering insulin is to state the number of units required and the strength per mil, e.g.:—

1,600 units insulin (protamine zinc)

80 units per mil

In this way ambiguity is impossible.

Recently a prescription was sent to us for:—

Insulin 200,000 units

On investigating this order for an abnormally large quantity of insulin,

PHYSICIANS' PRESCRIPTIONS

This article has been contributed by invitation and will be appearing in the PHARMACEUTICAL JOURNAL as well as in THE PRACTITIONER. It discusses the difficulties of prescribing from three points of view: (1) from the National Health Insurance Pricing Bureau; (2) from a practising pharmacist; (3) from the dispensary of a large voluntary hospital.

I.—By JEAN K. IRVINE, M.B.E.

Superintendent, South Eastern N.H.I. Pricing Bureau; President, Pharmaceutical Society of Great Britain.

ONE of the greatest difficulties encountered by the pharmacist is bad handwriting. This sometimes amounts to complete illegibility, and it then constitutes a danger to the public, for the pharmacist may perhaps misinterpret the prescription. For instance, a prescription for Tab. phenaloin was read as Tab. phemitone, and one for P. glucosi was dispensed as Ol. jecoris. Tab. theominal has been interpreted as Tab. prominal, and Tab. thyroid sicc. as Tab. quinidin. This last example sounds incredible, but there was no doubt about the fact that Tab. quinidin was a reasonable interpretation of the doctor's writing. A rather more amusing instance occurred recently when the doctor ordered a mixture, stated the directions, and then, abandoning the familiar "mitte", wrote "Give ̄xii". The chemist read this as "Ol. olivæ ̄xii".

OUT-OF-DATE FORMULÆ

The prescribing of preparations in out-of-date formularies by their title only is a cause of much time being wasted by the pharmacist. Some years ago almost each district had its own little book of formulæ, and in one or two areas these are still prescribed by name. As the first National Formulary came into force in 1929, it is sometimes difficult to trace these old prescriptions; if they are ordered on a N.H.I. script, the formula has then to be copied on to the script for the pricing office. Confusion is often caused by the fact that preparations of the *British Pharmaceutical Codex*, 1934, previously included in the *British Pharmacopœia*, 1914, are prescribed under their B.P. name. Such an example is Ung. gall. c. opio B.P.C., often ordered as Ung. gall. c. opio B.P. '14. Several preparations of the B.P.C. 1923 are still ordered, such as Lotio boracis and Unguentum Lassar. Unfortunately, it is often discovered that, in fact, these preparations are not intended by the doctor, who requires Lotio acidi borici and Pasta Lassar respectively. In consequence the pharmacist is often misled. What a pity the prescriber does not keep his reference library up to date.

Another practice that should be deprecated is the copying of proprietary formulæ. The ingredients are usually numerous, and the quantities are expressed in percentages or parts, with the result that very awkward

PENICILLIN

Penicillin prescribing is still in its elementary stages, and this probably accounts for prescriptions which are difficult for the pharmacist to interpret. For example, the B.P. oculentum is sometimes ordered in quantities of one or two ounces. As oculentum penicillin is packed in small, specially prepared "oculentum" tubes, containing 60 grains or 5 grammes, it would be preferable if the doctor were to order in these quantities, so avoiding wastage of the material and ensuring greater likelihood of the patient's being able to retain his eye ointment in a sterile condition. The essential point for a doctor to remember in ordering penicillin is that the strength in units per mil or per gramme should be given. The percentage method is not a practical method by which to order, as the quantity required must then be calculated from the potency of the sample of penicillin used.

II.—By E. RATCLIFFE, M.P.S.

Practising Pharmacist; Consulting Pharmacist, Wembley Hospital.

The chief sources of queries in dispensing medical prescriptions include:—

Illegible writing: a real and acute problem to the pharmacist, particularly when the name and address of the patient are indecipherable. If the patient or his agent has to be asked his name or how his name is spelt, a doubt immediately arises in his mind whether the pharmacist is able to interpret the vital part of the prescription and whether he is in fact receiving what the doctor intended. This difficulty could be avoided if the name and address were always written in block letters. It is a difficulty which arises particularly in or near large cities where the population is partly nomadic and of international origin. When unusual medicaments or proprietaries are ordered, it is of considerable assistance to the pharmacist if the names are written in a clear and distinctive manner.

Queries arising from *incompatibility* and *out-of-date formulæ* do not often occur; a good reference book usually solves the latter problem, but hospital and private formulæ may cause difficulty, particularly if the hospital is not situated locally or is not well known. In such instances the formulæ should be written in full, and the prescriber would then be certain that his patient received the specific preparation he intended. These difficulties usually arise from prescriptions written by newly qualified practitioners or "locums", but occasionally a formula is quoted from a recent article in the medical press which has not appeared in abstract in the papers commonly read by the practising pharmacist. With the gradual disappearance of the "omnibus" mixture and the greater simplicity of modern prescribing, the frequency of incompatible preparations has decreased. However, prescriptions for ointments and oily lotions are still encountered which produce unsightly preparations and defy all efforts on the part of the pharmacist to produce an elegant preparation.

Overdoses cause little trouble, but unusual doses sometimes perplex the

it was found that the doctor had intended, and the pharmacist had dispensed, penicillin, 200,000 units.

PROPRIETARY PREPARATIONS

Many difficulties exist in prescribing and dispensing proprietary preparations. One of the most common difficulties is because often the doctor orders a quantity that is not packed by the manufacturer. Hepamino, for example, a proteolysed liver preparation, is packed by the manufacturer in 5-ounce sealed bottles. What is the chemist to do if the doctor orders ̄viii ? Is he to open another bottle and dispense the extra quantity from it, give one original bottle, or, nearer to the requirement of the doctor, dispense two unopened packs? Were the prescription made out for "Hepamino, one bottle", the difficulty would not arise. Tablets also provide another cause of confusion if the number ordered by the doctor does not conform to the number in the pack as sent out by the manufacturer. The National Health Insurance Drug Tariff does, of course, make provision for such contingencies by allowing the chemist to claim for the cost of the next larger pack, provided he forwards to the Pricing Bureau the particulars of his claim and the Bureau considers such claim to be reasonable. Nevertheless, it is a wasteful method of prescribing. Examples are numerous: the following prescriptions present such problems:—

Anahæmin 20 c.c. vial

This preparation is packed in 15-mil and 30-mil vials only.

Colloidal Calcium c. Ostelin 15 c.c.

Again the manufacturer's pack is a 30-mil vial; no 15-mil vial is available

Aludrox ̄xvi

This preparation is not supplied in a 16 fl. oz. size, and is not easily manipulated, so that considerable waste occurs in dispensing.

REPEATS

The issue of "repeat" prescriptions by panel practitioners is prohibited, the purpose behind the prohibition being, of course, to obviate the necessity of looking up previous prescriptions issued for the patient. As copies of National Health Insurance scripts are not usually kept by the pharmacist such a search would in all probability take up a considerable amount of time. Legally, it is not necessary to retain National Health Insurance scripts for Fourth Schedule poisons; the patient has to give up the script before receiving his medicine, and as a consequence he cannot get a further supply without paying another visit to his doctor. Scripts for National Health Insurance patients receiving Fourth Schedule drugs are often incomplete; doctors omit either the address of the patient, or, more often, the quantity to be dispensed. Stricter attention to such details should be paid by medical practitioners, especially as prescriptions for hypnotic drugs are increasing in number.

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Queries arising from *incompatibility* and *out-of-date formulæ* do not often occur; a good reference book usually solves the latter problem, but hospital and private formulæ may cause difficulty, particularly if the hospital is not situated locally or is not well known. In such instances the formulæ should be written in full, and the prescriber would then be certain that his patient received the specific preparation he intended. These difficulties usually arise from prescriptions written by newly qualified practitioners or "locums", but occasionally a formula is quoted from a recent article in the medical press which has not appeared in abstract in the papers commonly read by the practising pharmacist. With the gradual appearance of the "omnibus" mixture and the greater simplicity of modern prescribing, the frequency of incompatible preparations has decreased. However, prescriptions for ointments and oily lotions are still numerous which produce unsightly preparations and defy all efforts on the part of the pharmacist to produce an elegant preparation.

Unusual doses cause little trouble, but unusual doses sometimes perplex the

it was found that the doctor had intended, and the pharmacist had dispensed, penicillin, 200,000 units.

PROPRIETARY PREPARATIONS

Many difficulties exist in prescribing and dispensing proprietary preparations. One of the most common difficulties is because often the doctor orders a quantity that is not packed by the manufacturer. Hepamino, for example, a proteolysed liver preparation, is packed by the manufacturer in 5-ounce sealed bottles. What is the chemist to do if the doctor orders ̄viii ? Is he to open another bottle and dispense the extra quantity from it, give one original bottle, or, nearer to the requirement of the doctor, dispense two unopened packs? Were the prescription made out for "Hepamino, one bottle", the difficulty would not arise. Tablets also provide another cause of confusion if the number ordered by the doctor does not conform to the number in the pack as sent out by the manufacturer. The National Health Insurance Drug Tariff does, of course, make provision for such contingencies by allowing the chemist to claim for the cost of the next larger pack, provided he forwards to the Pricing Bureau the particulars of his claim and the Bureau considers such claim to be reasonable. Nevertheless, it is a wasteful method of prescribing. Examples are numerous: the following prescriptions present such problems:—

Anahæmin 20 c.c. vial

This preparation is packed in 15-mil and 30-mil vials only.

Colloidal Calcium c. Ostelin 15 c.c.

Again the manufacturer's pack is a 30-mil vial; no 15-mil vial is available

Aludrox ̄xvi

This preparation is not supplied in a 16 fl. oz. size, and is not easily manipulated, so that considerable waste occurs in dispensing.

REPEATS

The issue of "repeat" prescriptions by panel practitioners is prohibited, the purpose behind the prohibition being, of course, to obviate the necessity of looking up previous prescriptions issued for the patient. As copies of National Health Insurance scripts are not usually kept by the pharmacist such a search would in all probability take up a considerable amount of time. Legally, it is not necessary to retain National Health Insurance scripts for Fourth Schedule poisons; the patient has to give up the script before receiving his medicine, and as a consequence he cannot get a further supply without paying another visit to his doctor. Scripts for National Health Insurance patients receiving Fourth Schedule drugs are often incomplete; doctors omit either the address of the patient, or, more often, the quantity to be dispensed. Stricter attention to such details should be paid by medical practitioners, especially as prescriptions for hypnotic drugs are increasing in number.

PENICILLIN

Penicillin prescribing is still in its elementary stages, and this probably accounts for prescriptions which are difficult for the pharmacist to interpret. For example, the B.P. oculentum is sometimes ordered in quantities of one or two ounces. As oculentum penicillin is packed in small, specially prepared "oculentum" tubes, containing 60 grains or 5 grammes, it would be preferable if the doctor were to order in these quantities, so avoiding wastage of the material and ensuring greater likelihood of the patient's being able to retain his eye ointment in a sterile condition. The essential point for a doctor to remember in ordering penicillin is that the strength in units per mil or per gramme should be given. The percentage method is not a practical method by which to order, as the quantity required must then be calculated from the potency of the sample of penicillin used.

II.—By E. RATCLIFFE, M.P.S.

Practising Pharmacist; Consulting Pharmacist, Wembley Hospital.

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that a patient may continue to obtain barbiturates over periods extending to years without again consulting the physician.

Whilst the instances and types of difficulties enumerated may appear to constitute a formidable list, only a very small percentage of prescriptions present great difficulty in everyday practice. The instances given represent difficulties encountered over a long period and in several areas in the country. Generally, it will be found that intelligent interpretation on the part of the pharmacist and confidence on the part of the prescriber in the pharmacist, with good will and cooperation on both sides, will remove the majority of difficulties, and the small residue usually arises from prescriptions being presented by patients whose physicians are resident in other areas.

III.—By J. BARCLAY HOUGH, M.P.S.

Deputy Chief Pharmacist, Royal Gwent Hospital, Newport, Mon.

During the 18th century the physician's practice of communicating his instructions to the apothecary by word of mouth fell into disuse, and it became customary to give written instructions in the form of a prescription. Throughout the years, physicians' prescriptions have varied considerably, but it may truly be said that they function as a mirror in which is reflected current medical thought and opinion. Although two-and-a-half centuries have passed since their origin, the compounding of physicians' prescriptions remains the most distinctive and important branch of the profession of pharmacy. Marked changes have taken place during the last twenty-five years in the methods of treating disease, and it is a far cry from the opiates, antimonial emetics and calomel, commonly prescribed at the beginning of the 19th century, to the sulphonamides, synthetic oestrogens, and vitamins prescribed to-day. Some authorities believe that the writing of prescriptions is fast becoming a "lost art" and the *Pharmaceutical Journal* stated in 1944: "It is, however, clearly evident that here, as in America, prescription writing has been allowed, indeed it has been encouraged to deteriorate . . . Its revival is the concern, not only of the physician, but also of the pharmacist". The hospital pharmacist, in virtue of his close professional contact with the medical staff of his institution, occupies a unique position, enabling him to give valuable counsel and guidance in the way to avoid the common pitfalls and difficulties in prescription writing.

Perhaps the greatest difficulty, and one which is not confined to hospital prescribing only, is the problem of the illegible prescription. It is an axiom that correct interpretation of a prescription depends entirely upon clear handwriting. On February 13, 1936, in the House of Commons, the Home Secretary was asked (*Parliamentary Debates*) whether he would consider action to ensure that prescriptions should not be dispensed unless easily legible. He replied that he had no information that would lead him to suppose that the practice referred to was prevalent or had been productive of any harm to the public. Unfortunately, examples which have been

pharmacist, and it would help him if these were initialled by the prescriber, especially when they are substantially higher than the usual dose. Thus, a prescription for 5-grain doses of sodium phenobarbitone would raise a doubt in the mind of a pharmacist; although this does not represent an overdose, it is an unusual dose, but if initialled by the prescriber the pharmacist would dispense it without hesitation. Apparent overdoses may have become normal doses for individual patients, so that when a prescription is taken to a pharmacist who is unfamiliar with the idiosyncrasy of the individual, he is reluctant to dispense a quantity ordered, e.g., a patient may have become accustomed to a 10-minim dose of liquid extract of stramonium.

As a result of war-time difficulties some *proprietary medicines* are still in short supply, and if the prescriber would bear this fact in mind he might advantageously prescribe an official alternative on the prescription. When necessary the strength of proprietaries should be stated. Often it is found that different strengths are made, and the pharmacist must get in touch with the prescriber before dispensing the preparation. It would assist the pharmacist if manufacturers standardized the size of their packages; tablets, for example, might be packed in bottles containing 21, 42 and 84 tablets. Such packing would often save "broken bulk" in the pharmacy; the pharmacist would not be left with a few tablets nor the patient expected to pay part of the cost of a preparation he did not receive.

INCOMPLETE DIRECTIONS

It is often found that when a prescription states "to be taken as directed", the patient is not certain of the directions given verbally by the doctor. This applies especially to "sulpha" drugs when a large initial dose is ordered to be followed by doses varying in strength and frequency. When the directions are entirely omitted the patient often wonders whether it was a teaspoonful, dessertspoonful or tablespoonful which was ordered, whether the preparation was to be taken before or after meals, or whether it should be taken in water.

The Dangerous Drugs Acts, the Fourth Schedule of the Poison Rules, and the Penicillin Act are sometimes more honoured in the breach than in the observance. The practitioner may think that the pharmacist is over-cautious and too punctilious, but the regulations are rigid and the penalties for non-observance heavy. This applies more particularly to repeat prescriptions; for dangerous drugs and penicillin "repeat as required" or "repeat weekly" are not valid directions, as the prescriber must endorse the prescription for a specific number of repeats or at specified intervals within a fixed period. It must be emphasized that prescriptions for dangerous drugs can only be repeated twice, that is, three times in all. With Fourth Schedule drugs, if the address of the patient is not given, this omission makes the prescription irregular. Repeat prescriptions must be so endorsed by the prescriber, and it is preferable for the exact number of times on which the prescription may be repeated to be stated clearly. Experience has shown

following prescription:—

	per cent.
Zinc oxide	2.23
Acid boric	2.05
Menthol	0.515
Adeps lanæ anhyd.	10.56
Paraff. molle ad	100 per cent.
M.ft.ung.Sig. m.d.u	

The therapeutic efficiency of this preparation is not improved by stating the amounts to two and three places of decimals and there can be no objection to approximating the values as follows:—

	per cent.
Zinc oxide	2.2
Acid boric	2.0
Menthol	0.5
Adeps lanæ anhyd.	10.5
Paraff. molle ad	100

This type of prescription should be avoided in rational prescribing.

The similarity of the signs \mathfrak{z} i and \mathfrak{z} i in prescriptions is very misleading, and instances have occurred when these symbols have been confused, especially when the writing is defective. It is undesirable to employ symbols which cause confusion, and some years ago a suggestion was put forward by Dott (1935) to replace the \mathfrak{z} sign by the Greek Δ , which is distinctive, easily written and, being the initial letter of drachma, is not likely through lapse of memory to be written for the ounce. It is a great pity that this suggestion has not been allowed to develop. Hospital pharmacists would do well to bring to the attention of their medical colleagues the following statement which appears in the Pharmacopœia of St. Bartholomew's Hospital: "Signs \mathfrak{z} i and \mathfrak{z} i are apt to be misleading and should not be employed by prescribers: solids should be prescribed in grains (gr.) and ounces (oz. 437.5 grains), and liquids in minims (min.) and fluid ounces (fl. oz.). Roman numerals should not be employed. In order to avoid the possibility of confusion between gramme and grain, the symbol G. should be used in prescriptions as the contraction for the gramme". It is of interest to note that the same instruction appears almost word for word in the National (War) Formulary, Third edition.

The recommendations of the Inter-Departmental Committee on Medical Schools include compulsory hospital appointments for doctors after qualification, and before entry into independent practice. If this recommendation becomes effective there is no doubt that the hospital pharmacist will be able to exert a beneficial influence on the prescribing habits of practitioners at an early stage in their professional careers.

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 — (1935): *Ibid.*, 134, 56.
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 Stehle, R. L. (1942): *Canad. med. Ass. J.*, 46, 463.

described (*Pharm. J.*, 1935) as "calligraphic vileness among professional men and women" are becoming increasingly common, and it is a regrettable fact that the writing of illegible prescriptions is not a punishable offence in this country. The only solution to the problem seems to be a campaign for clear writing as suggested in the *Pharmaceutical Journal* (1946).

USE OF THE METRIC SYSTEM

The prescribing of drugs in the metric system is becoming increasingly popular in hospital practice, and this is particularly noticeable with the newer chemotherapeutic agents. In America, the Council on Pharmacy and Chemistry (1943) has announced that New and Non-official Remedies, Useful Drugs, the Epitome of the U.S. Pharmacopœia and National Formulary and Interns' Manual will give quantities and dosages exclusively in the metric system, and states that "the universal adoption of the metric system would be a manifestation of rationality and interprofessional and international cooperation of high practical utility". Some medical journals have decided to insert the metric equivalent parenthetically after each old style dose, weight and measure, and it is hoped that this will lead to the general use of the metric system in British medicine. At the present moment, while two systems are in use, it is not uncommon for prescriptions to contain a mixture of imperial and metric units, and hospital pharmacists should condemn this practice as being unorthodox and potentially dangerous, especially when abbreviated symbols are used. Stehle (1942) has also pointed out the anomaly of ampoules to be dispensed according to metric volume and imperial weights, e.g. "Ephedrinæ Sulphas, $\frac{3}{4}$ grain in 1 c.c.". There seems very little doubt that the time will come when the metric system will be universally used. In anticipation of this state of affairs the hospital pharmacist should familiarize himself with the metric doses of drugs, as difficulties are bound to occur during the transition period.

When the metric system is employed the terms "millilitre" (mil) and "cubic centimetre" (c.cm.) almost invariably give rise to confusion. In an analysis of 20 prescriptions written in the metric system recently by hospital physicians only three contained the correct term of "millilitre". The *Pharmaceutical Journal* (1933) goes so far as to say that "in 99 instances out of 100 when the term 'c.c.' is used the millilitre is meant". The term "c.c." is hard to kill, and when one-thousandth part of a litre is intended the millilitre (mil) should always be used. Although for practical purposes there is very little difference between the c.cm. and the mil, it should be argued that correct scientific terms should be employed when writing a prescription.

PERCENTAGE DIFFICULTIES

In hospital prescribing the proportion of ingredients in a prescription is very often stated as a percentage, particularly in the case of ointments, and lotions. A difficulty which sometimes occurs may be illustrated by the

moderate meals, is becoming increasingly common. Among the infants developing the lymphoid-catarrhal condition already described, vomiting or an attack of coughing may cause sudden and profound collapse (Evans, 1946).

Gastro-intestinal disturbances.—During the past twelve months a peculiar relationship between certain conditions and the taking of fruit, fruit products or certain vegetable foods, e.g. tomatoes and rhubarb, has become apparent. At first a marked increase in cases of gastro-enteritis only was noted, but later a close relationship was found between the ingestion of fruit and the onset of some acute infective conditions. Minor rheumatic conditions have shown a similar causative relationship. In the gastro-intestinal type, a characteristic blanching of the tongue and the passage of clay-coloured stools with only a slight degree of jaundice were suggestive of a toxic hepatitis. It had previously been noted that breast-fed infants suffering from steatorrhœa and other intestinal disorders were adversely affected by the taking of marmalade by the mother.

Intensive research among sick and healthy people revealed the fact that susceptibility to fruit varied more or less directly with the degree of dependence upon margarine as a fat supplement. Investigation of infants and children in the light of this fact showed that those most susceptible to fruit or fruit juices were of the lymphoid-catarrhal type, and were born of mothers who had depended upon margarine during pregnancy. It was also noted that both the lymphoid-catarrhal change and the susceptibility to fruit were aggravated by a number of foods containing either calciferol, vitamin D₂, or "added vitamin D". These findings have consistently received confirmation during the past three months, and the removal from the diet of foods containing "added vitamin D", although involving further restriction of fat in the case of adults, has been justified by results in most cases, often without the necessity for active treatment.

THE VITAMINS AND RESISTANCE TO INFECTION

THE practical approach to the problem under investigation was based on the effects of *vitamin K* analogue and *nicotinic acid* in a number of minor conditions. The known importance of the vitamins in food suggested their use as interdependent factors in maintaining the natural mechanisms of defence against, and recovery from, infective and inflammatory conditions. The B complex was first considered, and dried non-autolysed brewer's yeast was chosen as the most convenient source. Its use with vitamin K analogue was immediately encouraging, bringing about rapid resolution in acute suppurative conditions, and reducing the amount and duration of suppuration (case I). Certain types of gastritis were greatly benefited by the use of vitamin K with vitamin C and yeast. Pyrexial cases were also found to be controlled rapidly with the aid of yeast and vitamin K, except in tuberculosis, in which the latter vitamin is not tolerated well; whilst yeast seems to supply an even greater need than in other conditions.

Vitamin P was first tried in minor rheumatic conditions in which swelling

FURTHER NOTES ON THE USE OF VITAMIN K IN GENERAL PRACTICE

By D. MARCUS EVANS, M.R.C.S., L.R.C.P.

IN an article on the use of vitamin K in general practice (Evans, 1946) reference was made to certain changes in the nature of some common conditions. During the past eighteen months, the changes mentioned have progressed. This general downward trend in health seemed sufficiently definite and serious to justify further research along the lines suggested by the results of earlier experiments with vitamin K analogue.

RECENT EVIDENCE OF VITAMIN IMBALANCE

In addition to the lowering of respiratory and cutaneous resistance to infection previously described, a further insidious change has been noted in such cases, particularly in infants and young children, i.e., a tendency to the development of general shotty *enlargement of superficial lymph glands*, in some cases this being present at birth. Various degrees of gastro-intestinal dysfunction have been found in association with this lymphatic-respiratory change. In other age-groups the lymphatic system seems to be involved more readily than formerly in cases of sepsis. Treatment of these glandular conditions with vitamin A as fish-liver oil has gradually lost effect, later requiring the addition of aneurine which, in turn, has become ineffective.

Various *hæmorrhagic conditions* have been more frequent, such as spontaneous subcutaneous and subconjunctival hæmorrhages, and also epistaxis and hæmoptysis in the mildest respiratory conditions. Treatment of these cases with vitamins K, C and P has been unsatisfactory. Minor conditions attributable to deficiency of the vitamin B complex, such as cheilosis, glossitis, corneal vascularization and peripheral neuritis, are more common and are not now adequately controlled by the B complex alone.

Among physiological changes, *dentition in infants* and *growth* periods in older children, whilst progressing satisfactorily in respect of rate and amount of dental and skeletal development, require greater care and supervision. An unusual number of infants show completion of the first dentition by the age of sixteen to eighteen months.

In *pregnancy*, the milder forms of toxæmia seem more prevalent, whilst post-partum debility is more common and pronounced, with greater liability to breast infections.

Nervous phenomena.—Anxiety neurosis, the effort syndrome, and a fatigue state similar to that ascribed by Scarborough (1940) to deficiency of vitamin P, are now more frequent among active and otherwise healthy adults. Nervous instability of various kinds, such as dizziness and flushing on changing position, or flushing, perspiration and drowsiness after

diaphoretics, vitamin K, nicotinic acid and yeast in various combinations. The temperature ranged between 99.8° F. (37.7° C.) and 101.6° F. (38.3° C.).

On January 27 he was given a quarter-tablet of vitamin P (hesperidin) (37.5 mgm. approx.) during the evening. The patient slept all night for the first time and the pain practically disappeared. The joints were still tender but swelling was greatly reduced. The temperature was 97.6° F. (36.4° C.) and did not again rise above normal during the illness. Vitamin P, 37.5 mgm., was continued twice daily.

January 31. Movements were free and gave little pain. The patient was otherwise well. On February 2 he got up and complained only of stiffness in the joints. He resumed work after a further week.

Case III.—M.P., aged sixty-two. March 26, 1947. She had had acute left lumbar pain for the preceding three weeks; she was limping and there was swelling and acute tenderness over the left lumbar posterior spinal muscles.

At 8 p.m. the patient was given vitamin K, 5 mgm., and vitamin P, 37.5 mgm., to be repeated morning and night. The next evening she looked happy, was walking erect and felt much better, and stated that the pain had been so much better that morning that she had taken a double dose (vitamin K, 10 mgm., and vitamin P, 75 mgm.). The original dosage was continued twice daily for two days as the muscles were still tender although swelling had almost disappeared. No further treatment was found necessary.

Case IV.—M.W., aged twenty-one. On March 14, 1947, she was taken ill with acute pleurisy without effusion. Temperature, 103.2° F. (39.55° C.), pulse rate, 100. At 11 p.m. she was given vitamin K, 10 mgm., and nicotinic acid, 50 mgm., immediately, and a dose consisting of nicotinic acid, 50 mgm., and yeast, 10 grains (0.65 gm.), four hours later. She slept a little, and next morning the stabbing pains were less severe and the dry cough less frequent. Temperature, 100.1° F. (38.3° C.), pulse rate 90. She was given vitamin K, 5 mgm., twice in the day and nicotinic acid, 50 mgm., with yeast, 10 grains (0.65 gm.), three times in the day.

March 16. She slept all night. There was pain only on coughing, which was infrequent. Temperature, 98.2° F. (36.8° C.), pulse, 80. The patient was allowed a milk diet and was given yeast, 10 grains (0.65 gm.), three times a day.

March 18. She was eating and sleeping well, was free of signs and symptoms and was allowed up. Yeast, 10 grains (0.65 gm.), was continued twice daily until she went out on March 20. She now enjoys better health than for some years previously.

Case V.—F.C.T., aged one year and two months. When three weeks old was operated on for intussusception and ever since had suffered from intractable vomiting; cow's milk and various dried milk foods having been tried in turn, one of the latter still being taken. Mucus was vomited and passed in the stools which were greenish-black and of liquid consistency. The vomit occasionally contained "coffee-grounds". The child had not passed a restful night for several months.

On June 19, 1947, when first seen, the child was pale, thin, poorly developed and quite unable to sit up. Signs of upper respiratory catarrh were present and there was general shotty enlargement of superficial lymph glands. Six teeth had erupted. The abdomen was distended but not doughy. The weight was 11 lb.

An initial dose of vitamin K, 10 mgm., was given, followed in two hours by vitamin E, 1.5 mgm., vitamin P, 37.5 mgm., and yeast, 10 grains (0.65 gm.), this dose to be repeated three times the next day and twice daily thereafter. Four ounces of diluted cow's milk with added sugar were given every four hours.

On June 26, the child was happy, kicking his legs about and making feeble attempts to sit up. He had slept soundly every night and vomiting had ceased after the second day when much mucus had been brought up. The stools were yellow and abdominal distension was less. Treatment was continued, and feeds increased to 6 oz. (170 c.cm.), and strengthened to a two to one ratio of cow's milk to water.

July 3. The child was stronger, used his limbs freely and weighed 14 lb. Vitamin E, 0.75 mgm., vitamin P, 37.5 mgm., yeast, 10 grains (0.65 gm.), and vitamin B (aneurine), 0.75 mgm., were given twice daily. Three drops of concentrated fish-liver oil were given daily.

July 8. A tooth erupted. Colour improving. Vitamin C, 5 mgm. daily, added.

was a prominent feature (cases II and III). It also appears to have a beneficial effect on pyrexia and in some cases of hyperchlorhydria.

Vitamin E also has some effect on pyrexia, apparently controlling delirium. It has been found to be effective in aiding localization of closed or open infective foci.

Vitamin A, which might be expected to improve the glandular, nervous and epithelial changes, has not proved effective, possibly, as discussed later, owing to faulty absorption.

Vitamin C has had effects difficult to understand, causing severe local and constitutional disturbance in cases of rheumatoid arthritis and in pyrexia, its effects approximating closely to the vitamin P deficiency syndrome already mentioned. It has been beneficial in some apyrexial, localized infective conditions when used with vitamin K and yeast.

Requirements of *vitamin B₁* seemed to increase during the early part of the war, but during the past three years this vitamin has gradually developed a peculiar tendency to cause relapse in certain types of illness, particularly in cases of neoplasm and in chronic respiratory disease, including pulmonary tuberculosis. In such cases, a single subcutaneous injection of 25 mgm. of thiamin was followed within six days by a dangerous relapse of the original condition with the appearance of a superimposed condition of nervous exhaustion and collapse. An almost identical effect was noted after injections of calciferol with colloidal calcium, an initial remarkable relief of symptoms being followed within six days by a rapid deterioration of the patient's condition.

CASE RECORDS

In the following case records vitamin K, vitamin E and yeast should be taken to represent acetomenaphthone, synthetic racemic α -tocopherol acetate, and dried non-autolysed brewer's yeast, respectively.

Case I.—J.M., aged fifty. May 6, 1947. Large carbuncle on the left wrist, discharging slightly through three small stomas. Swelling and redness extended over the dorsum of the hand. Three red lines of lymphangitis ran up to the elbow, and the axillary glands were swollen and tender. The patient was ill but apyrexial. A first dose of vitamin K, 10 mgm., vitamin E., 0.75 mgm., and yeast, 10 grains (0.65 gm.), was given, followed by vitamin K, 2.5 mgm., vitamin E, 1.5 mgm., and yeast, 10 grains (0.65 gm.), every four hours night and day. Next day he felt better and had spent a comfortable night. The carbuncle discharged freely through a single stoma and swelling of the hand had disappeared. Only a faint trace remained of the lymphatic infiltration. The axillary glands were smaller and less tender. The vitamin combination was continued four-hourly during daytime only. Two days later only a small, shallow, clean ulcer remained. The axillary glands were smaller and no longer tender. The vitamins were continued three times daily until May 11, and the patient went to work on the next day.

Case II.—J.R., aged forty-six. On January 18, 1947, he had perspired rather freely at work and felt chilly next day.

January 20. He was taken ill with acute pain and swelling of the right ankle and acromio-clavicular joints which completely prevented movement of the arm and leg. Temperature was 102.6° F. (39.2° C.). The joints were acutely tender. For the next seven days the condition was practically unchanged in spite of salicylates,

DRAINS AND HEALTH

By A. G. G. THOMPSON, M.D., D.P.H.

Medical Officer of Health, Borough of Lambeth.

ONE HUNDRED years ago, drains (the property and responsibility of the house owner) and sewers (the responsibility of the local sanitary authority) of the kind to be found to-day in all built-up areas were quite unknown. Many houses, particularly in the poorer quarters, had no drains at all, others had short drains to cesspits which were usually filled to overflowing and for which nobody, literally nobody, undertook any responsibility either for emptying or repairing, or indeed for any form of maintenance. The smells and the danger of contamination to the shallow well water must both have been prodigious, but everybody was no doubt so accustomed from birth to fetid odours that not until Edwin Chadwick and other reformers in the early years of the last century forced public opinion to take notice was anything done.

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THE RISKS OF INFECTION

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July 12. The stools had been loose but yellow for two days. Vitamin C, vitamin B, and fish-liver oil were stopped, and vitamin E again increased to 1.5 mgm. twice daily, with vitamin P and yeast as before.

July 28. The baby was normal, except for the glandular enlargements which were only slightly smaller, and weighed 16 lb. 2 oz. Treatment was continued for a further four weeks, when a varied diet was gradually introduced without mishap.

DISCUSSION

The nature of the changes detailed in the first part of this article seem to constitute evidence of the existence of a progressive multiple vitamin-deficiency state. The effectiveness of acetomenaphthone and synthetic α -tocopherol acetate, water-soluble and rapidly absorbed substitutes for natural vitamin K and vitamin E respectively, in conditions susceptible to those changes, suggests that this vitamin-deficiency state is due to faulty absorption of the fat-soluble vitamins. The observed toxic effects of fruit, pointing to a pre-existent subclinical derangement of liver function, include an abnormal sensitivity of the biliary function of the liver. This may explain the failure of dietary and orthodox therapeutic supplementation with natural vitamins to check the progress of events, since the absorption of the fat-soluble vitamins A, D, E and K depends upon the presence of healthy bile in the intestine (Bicknell and Prescott, 1946).

Regarding the causation of this presumed failure of efficient secretion of bile, the unique position occupied by vitamin D is significant in that its widely used analogue, calciferol or vitamin D₂, is water-soluble and rapidly absorbed. The administration of a single vitamin, even in reasonable amounts, may induce or aggravate signs of deficiency of one or more other vitamins, and therefore the preferential absorption of vitamin D₂ over that of the other fat-soluble vitamins might, even in normal circumstances, initiate a complex conditioned deficiency state comparable with that which seems to exist. The absence of rickets from the list of deficiency states described is also significant.

The favourable results of restriction of intake of margarine in adults and of foods containing vitamin D₂ in infants, although not statistically represented here, are suggestive of a common factor contained in these foods. The exact identity of the vitamin D in margarine is not ascertainable (Bicknell and Prescott, 1946), but the above considerations would seem to indicate its probable nature. Both calciferol and natural vitamin D are known to be toxic in large amounts, but the effects of prolonged administration of small doses have not to my knowledge been reported and, from consideration of the evidence submitted, may conceivably be detrimental.

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DRAINS AND HEALTH

By A. G. G. THOMPSON, M.D., D.P.H.
Medical Officer of Health, Borough of Lambeth.

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the belief, still widely held, that bad smells are themselves the danger and can "breed a fever". It is certainly true that decomposing animal matter, or in particular a defective drain allowing air from the drains to enter the house, does lead to ill-health in the form of mild headaches and relaxed throats, but the air in sewers is not such as to render the work of sewer-men who have to work in such atmospheres any more dangerous on that account. In fact, the only added danger in such employment is the increased risk of contracting Weil's disease, through the spirochætes passed by the brown rat penetrating the skin of the sewer-men if damaged or abraded in the course of their work. A chronic sore throat, however, is at least more likely to offer better opportunities of thriving to such infections as scarlet fever and diphtheria, but it cannot, of course, actually "breed the fever". In the past many cases of infectious diseases have been associated with defective drains and advantage is taken of the fact nowadays to test the drains whenever a notification of infectious disease in the house is received by the Medical Officer of Health. In that way an unobtrusive improvement is continually pressed forward in the general environmental conditions without making a dead set upon drains as such. Drain defects are generally expensive to repair and take time so far as owners are concerned, and when discovered are apt to weigh unduly upon the minds of the occupiers who have to put up with delay, so that a deliberate search for defective drains over a wide district is not practicable.

The brown rat is a natural inhabitant of the sewers, where he finds the environmental conditions as well as food and water both plentiful and to his liking. Nesting facilities, however, are not so good in the sewers and so rats enter the drains from which they can escape through defective joints and broken drain pipes to find more secluded and drier nesting places above ground. In town the presence of brown rats (*Rattus Norvegicus*) is an indication of some fault or defect in the sewerage, such as a broken or disused drain or an unsealed opening, and this exit is the most important discovery which must be made before rat infestation can be permanently abated.

THE MODERN DRAINAGE SYSTEM

The drain should remove all waste liquids and foul water from the premises to the sewer and should prevent anything from travelling in the reverse direction from the sewer through the drain to the house. This one-way traffic is largely achieved, apart from the force of gravity, by water-sealed traps. Every pipe opening into a drain is furnished with a trap which is effected by giving that pipe a double bend before connecting it with the drain. Examination of the waste pipe from a sink or wash basin will reveal this bend and in it there is always to be found water standing just as there is in every water closet, acting as a barrier to prevent odours from the drain

entering the room. After a house has stood empty for a time the water in the traps will evaporate and the seal is then broken. A musty unpleasant smell due to this is often experienced on returning home after a summer holiday. Open the windows then by all means but do not neglect to pull the chains everywhere and turn on all the taps for a few moments to reinstate the water seals. Occasionally the air pressure in the drain rises and sewer gas might then bubble through a trap if it were not for the fact that every modern drain is properly ventilated by a fresh air inlet, usually with a mica flap situated at the sewer end of the drain, which allows air to enter but not to return, and one or more vent pipes at the top end of the drain, which project some three feet or so above the eaves and are usually capped by spherical wire cages to prevent birds' nests, tennis balls or other objects from blocking the free flow of air. At least one rainwater pipe too, will be found to discharge near the top of the drain to insure an occasional scouring right through with clean water. It is customary to place a water-sealed trap, called an interceptor, between the house drain and the sewer to prevent sewer gas from entering the house drain and to impose an additional obstacle against rats, but this is not by any means the rule. The practice of doing without the interceptor is connected with the ventilation of the sewer, the idea being that each house vent pipe will ventilate its own stretch of sewer. Unhappily this does not always follow and occasionally one vent pipe is found acting as the exit and all others in surrounding houses acting as fresh air inlets. Complaints of smells from this one vent pipe will then swiftly follow.

Any complaint regarding the inadequacy or inefficiency of a drain should be addressed to the Public Health Department, to the Medical Officer of Health or to the Sanitary Inspector of the local sanitary authority whose duty it is to deal with such things, and not to the Engineer or Surveyor of the authority, whose responsibility begins at the connexion of the drain with the sewer and may go on from there right through the sewerage system to the purified effluent from the sewage farm where it enters the natural water-course on its way to the sea. Before invoking the aid of the local sanitary authority it is, of course, only courteous to inform the owner or agent who collects the rent and give him an opportunity to right any defect, since the great majority of owners are alive to their responsibilities and anxious to maintain their property in good order.

It is only common sense to see that drains are used properly, but unhappily this is by no means the case. Drains have been blocked with bread which someone was afraid to put in the pig-bin in case a Ministry of Food official might notice and prosecute. Sanitary towels are frequently the cause of obstruction, particularly in businesses where many girls are employed, and inquiries have established the fact that ignorance and shyness are the two principal reasons for such conduct. Sometimes a bad tenant clearing

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The effluent after leaving these beds is clear and odourless, but, of course, still contains organisms such as *Bacillus typhosus*, which survives the sewage treatment and can be found in most effluents of large towns, from the typhoid-carrier inhabitants. It can usually be released without danger into a natural watercourse after a final aeration over an artificial waterfall or two but, particularly in summer weather, there is usually a fairly heavy growth of humus, a grey scum sometimes called "sewage fungus", which breaks down and decomposes, absorbing the oxygen content of the effluent in doing so. The water condition then becomes incompatible with life, either of fish or weed, so the humus is skimmed off the surface in humus tanks before it can decompose and is then pumped back to the sludge digesters while the effluent flows on to the discharge point. The digested sludge is drawn off from the bottom of the digesters from time to time and pumped on to the land, where the water separates easily without nuisance from the drying sludge, which is then ploughed in and the land cropped.

It will be seen that the whole process is nothing but a modified form of the natural happenings undergone by any decomposable matter in water, aided by heat and additional aeration plus the highly intensified effect in a short time of the aerobic organisms and *psychoda* in the sprinkler beds. The working is simple and easy when everything is running smoothly, but constant attention is needed. The quantity of activated sludge required by the incoming fresh sewage, for example, must be frequently checked, as the strength of sewage depends so much upon rainfall. The many various wastes from different trades can also exercise marked effects, as will be readily understood when it is remembered that sewage treatment is really carried out by living bacteria. The antiseptic action of some wastes can be strong enough to put out of action the sprinkler beds, which will then take some time to recover. Other wastes absorbing oxygenating powers unduly can also throw the bacterial action out of gear. In this connexion, the milk wastes from creameries, butter and cheese factories are extremely difficult as they require some 150 times as much oxygen as an ordinary average sewage. They are accordingly dealt with before entering the drains by a chlorination process. The housewife should not therefore put disinfectant down the drains, because in the first instance it is a complete waste of money and material and, secondly, it tends to paralyse the action of the bacterial beds.

SEWAGE AND WATER SUPPLY

In rural districts where the water supply is drawn in a bucket from a stand pipe or well, or is pumped from a well into a house, there is no arrangement for the disposal of sewage beyond a cesspit in which a mixed anaerobic-aerobic decomposition takes place. Liquid products of decomposition escape through the overflow and being away from dwellings cause no nuisance.

out from a bad landlord will deliberately stop a manhole with old brushes, rags, bricks and other solid material, and the incoming tenant after a week or two's occupation is the sufferer.

THE DISPOSAL AND USES OF SEWAGE

The disposal of sewage by modern methods after it has left the house drain is a fascinating study of success in improving upon Nature's own ways of dealing with decomposing material. Sewage is really nothing more than a vast bulk of water conveying a small quantity of solid (some 50 parts in 100,000) and liquid impurity, and the first process is to allow as much of the solids to settle out as will do so. This sludge, as it is called, is pumped to the digestion tanks where it decomposes under anaerobic conditions with the production of methane 60 per cent., carbon dioxide 30 per cent., and other gases. This mixture is of considerably higher calorific value than coal gas to-day, and is used in gas engines to drive dynamos which produce all the power and light needed on the sewage farm. The gas can also be compressed to some 4000 to 5000 atmospheres and can then be used instead of petrol to drive all the house dust collecting and street cleansing vehicles of the local authority. The sludge is kept warm in the digesters by the water from the jacket of the gas engine, which is cooled in that way instead of by radiators. The digesters work at about 85° F. The gases produced by a similar process of decomposition at the bottom of ponds have been known for centuries as marsh gas, which is on occasion spontaneously ignited when reaching the air. It is the origin of marsh lights or "Will o' the Wisp", and was looked upon as a machination of the Devil to lure benighted travellers into the swamps.

Turning back to the sewage from which the sludge has been settled, this now undergoes artificial aeration as it flows slowly through tanks with porous bricks at the bottom, through which compressed air is forced, escaping into the sewage in finely divided bubbles. The natural oxidation process receives tremendous stimulation from this artificial aeration and the decomposable contents of the sewage are rapidly broken down. The sewage is then allowed to stand in another settlement tank and deposits more sludge, most of which is pumped back to the digesters. Some, however, which has been highly activated by receiving a further treatment with compressed air, is returned to mix with the incoming sewage from the first sludge tank, inoculating it with a concentration of aerobic organisms. The aerated sewage from the second settlement tanks is now taken over continuous sprinkler beds where the force of gravity turns the long arms so that an even, continuous flow of sewage is sprinkled over the bed of coarse clinker which is impregnated with oxidizing organisms. The innumerable flies known as moth midges (*psychoda*) which breed in these sprinkler beds are also a great help in breaking down the decomposable contents of the sewage upon which the larvæ feed.

CURRENT THERAPEUTICS

IV.—THE CLOTTING OF THE BLOOD AND ANTICOAGULANTS

By REGINALD ST. A. HEATHCOTE, D.M. F.R.C.P.

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THE CLOTTING OF THE BLOOD

THE process whereby blood clots after it has been shed and thereby prevents excessive blood loss from small wounds has been a subject of investigation for a very long time, some of the earliest useful observations having been published as far back as 1772. Since that time many theories have been devised, and much experimental work performed, in which, however, there are many differences of opinion and many contradictions of fact. It is therefore almost inevitable that in an article of this type a somewhat dogmatic attitude should be adopted, and for these purposes the theory put forward by Morawitz in 1904 will be used as a general basis. At that date, the principal constituents of the blood plasma had been identified, and it was known that the blood would clot in the absence of the formed elements, the red and white cells, so that the process was essentially one concerning the blood plasma alone.

Morawitz postulated that there are present in the plasma three substances which are necessary for the clotting of the blood but which will not themselves give rise to coagulation, namely, fibrinogen, prothrombin, and ionized calcium salts. A fourth substance, thrombokinase (thromboplastin), which is released when blood is shed or the tissues injured, is required, in addition to these three, to cause the blood to clot. Further, he regarded the process as taking place in two stages, in the first of which prothrombin, in the presence of ionized calcium salts, is converted by thrombokinase into thrombin, and, in the second, thrombin converts the soluble fibrinogen into the insoluble fibrin. It is now recognized that the first stage, the production of thrombin by the action of thrombokinase on prothrombin, can take place in the absence of calcium ions, but only extremely slowly. There is good evidence that thrombokinase acts in a manner similar to, if not identical with, that of an enzyme, and the ions of calcium seem to play the part of a co-factor. Again, the action of thrombin is similar to that of an enzyme; in fact there is reason to think that it is actually a proteolytic enzyme. It has been shown by the use of the ultra-microscope that fibrin occurs in long needle-shaped crystals which form long filaments interwoven throughout the blood and mechanically entangling the formed elements of the blood. Later, *in vivo* as *in vitro*, these filaments contract, for reasons as yet unknown, so that the clot becomes smaller, and the serum is squeezed out from the interstices between these filaments.

The general principles of Morawitz's theory have been widely accepted, although there are differences of opinion as to some of the details. Taking it as a basis, however, it is clear that the process of clotting could be varied by changing the physical conditions or the proportions of the ingredients required. Thus, since cold delays the action of enzymes, and the actions of both thrombokinase and thrombin are similar to those of enzymes, it would

The water consumption is in the neighbourhood of two to five gallons a day for each occupant and the cesspit and overflow can cope reasonably well with this volume of sewage. When a piped supply is installed in the house, however, water consumption rises rapidly to some twenty to thirty gallons a head and the volume of sewage is quite beyond the capacity of the cesspit. Nuisance rises rapidly from the escape of raw sewage into the nearby ditch and stream, which may easily be overwhelmed. The oxygen content of the stream water is absorbed, all fish and plant life dies, and the water remains fouled for miles down-stream.

One important, and, in fact, indispensable, adjunct to a piped water supply is therefore an efficient sewage disposal scheme, and in the minds of many, even in high places, the difficulties of providing the latter are not thoroughly appreciated. Much of the water supplied in this country is derived from surface waters rather than from deep wells. Most of the water supplied by the Metropolitan Water Board is drawn from the Lee and the Thames, from which towns higher up have drawn water and into which sewage effluents are returned. There is a limit to the proportion of even a good sewage effluent which a natural watercourse can accommodate, and there would be grave danger in drawing for use too high a proportion of water from a stream or river if the sewage effluent is to be returned to it, especially if lower down the stream another town's water supply is taken. It is unpleasant to think that the water we drink in a populated country like England has quite probably been derived partly from a sewage effluent, but the same water from the sea *via* the sun's evaporation, clouds and rain must have been used over and over again since the earliest days of the earth's existence, and so long as the water is potable there is no need to dwell upon its past history.

SUMMARY

Briefly then, house drains if they are in good order and condition will readily take all the waste liquids poured in without allowing anything to escape in the reverse direction. If properly constructed and not abused, a drain is self-cleansing and requires no disinfectant, which, in itself, does harm rather than good by imposing an extra strain on the sewage works. If anything is out of order, or if there is a suspicion that the drain has been damaged, either through unpleasant smells, damp walls or the presence of rats, the owner or his agent should be informed at once; if nothing is done, then the Medical Officer of Health, whose name and address must, by law, be inserted in the rent book, or any official of the local council, should be informed, when steps will be taken to make a thorough examination and test.

most commonly brain or lung. As already stated, it is probably an enzyme, requiring ionized calcium salts as its co-factor. An increase in the stability of the blood platelets, or a reduction in their number, would evidently delay coagulation of the blood. It is now thought that the former factor is responsible for the extremely delayed clotting which occurs in hæmophilia. Again, deficiency in the number of the platelets may lead to the occurrence of purpura. It is believed that normally the platelets have the function of protecting the walls of the capillaries, so that in their absence, relative or complete, defects in these walls are liable to occur, with consequent bleeding into the tissues. It is by no means certain that all cases of purpura are due to deficiency in the number of platelets in the blood, but it has been observed that in some cases of toxic purpura, e.g., those sometimes following the administration of sedormid (allyl-isopropyl-acetylurea), there is a very marked decrease in the platelet count. Again, it has been found possible to produce an antiplatelet serum, and injection of this into animals has caused a condition resembling purpura hæmorrhagica.

ANTAGONISTS TO COAGULATION

Naturally, during life minor injuries are constantly being sustained, and presumably following such injuries small amounts of thrombokinase are formed and added to the blood. None the less, intravascular clotting does not occur or life would cease. It is possible to produce extensive and fatal intravascular clotting in animals by intravenous injection of adequate amounts of either an active thrombin or thrombokinase, and so it is clear that the blood in the vessels is in a state in which clotting can occur if conditions are favourable. The commonly accepted explanation is that there is in normal blood a small amount of an *antithrombin* which can neutralize the effects of the small amounts of thrombin that are formed after minor injuries. The antithrombin appears to be part of the albumin fraction of the blood proteins.

Many other substances are known which possess the power of neutralizing the action of thrombin. Bleeding continues from the incision made by the medicinal leech for some time after the animal has been removed, and from the buccal glands of that animal a powerful anticoagulant, *hirudin*, has been prepared commercially. It acts both *in vitro* and *in vivo*, and that it is an antithrombin is shown by the fact that if an excess of thrombin be added to hirudinized blood, clotting takes place very rapidly. It has been extensively employed in laboratory experimental work to prevent clotting in animals, but does not seem to have been used clinically. Some of the azo-dyes, e.g. Chicago blue 6B, and chlorazol fast pink B.K.S., are powerful anticoagulants, both *in vivo* and *in vitro*, probably acting also by neutralizing thrombin. As they are relatively non-toxic, they are often employed in laboratory work, but again have not been used clinically.

Heparin.—In practice, the most potent substance used as an antithrombin

be expected that cooling blood would retard its clotting, and this is in fact the case *in vitro*. It is well known that cold applied locally to a bleeding surface *in vivo* encourages hæmostasis, but this is not a contradiction because the effect of cold in this case is to cause a local vasoconstriction and consequent slowing of the rate of blood loss, and so to accelerate the arrest of hæmorrhage.

Fibrinogen is a protein belonging to the general group of the globulins. Its absence from, or a reduction in its concentration (normally 0.3 per cent.) in, the blood, would evidently lead to the abolition of or delay in the clotting of blood. Such a condition does occur in certain, fortunately rare, diseases, such as pseudo-hæmophilia hepatica. Fibrinogen is apparently formed in the liver, for its concentration is markedly reduced in animals following severe damage to or removal of the liver, whilst in aplastic anæmia there is no such reduction. Experimentally, it has been observed that the blood clots with great difficulty in phosphorus or chloroform poisoning in animals, in which the liver is seriously damaged, and in phosphorus poisoning in man also the blood remains fluid long after death. There is, however, no drug known which in non-toxic doses can reduce the fibrinogen content of the blood to any considerable extent.

Calcium is present in the blood plasma (it is almost entirely absent from the red cells) to the extent of about 10 mgm. per cent., of which one part, rather less than one-half of the total, about 4 mgm. per cent., is bound to the albumin fraction of the plasma proteins and is therefore indiffusible and un-ionized, whereas the remainder, about 6 mgm. per cent., is almost entirely in the ionized form. Such a concentration is, according to Quick, slightly in excess of the optimal proportion required for normal clotting. Whilst in some conditions, e.g., severe hypoparathyroidism, the blood calcium in the ionized form may be considerably lowered, interference with blood clotting does not occur, and it is in fact doubtful if continuance of life would be possible if the ionized blood calcium fell to such a level as to render clotting of the blood impossible.

Prothrombin, a protein with a carbohydrate prosthetic group, is formed chiefly in the liver, although there is evidence that it comes in part from the bone marrow. Its production is governed by the presence in the body of vitamin K, methyl-phytyl-naphthaquinone, and in the absence of this substance from the diet, or its non-absorption from the intestine, there may be a considerable degree of hypoprothrombinæmia. Vitamin K and its synthetic substitutes, menaphthone and acetomenaphthone, are not absorbed from the gut in the absence of bile salts, and this fact accounts for the bleeding tendency so well known in cases of biliary fistula or of obstructive jaundice.

*Thrombokinas*e is probably a complex of a protein and cephalin, one of the lipides. It can be prepared from blood platelets by cooling oxalated plasma to 0° C. for two or three days, but also from almost any animal tissue,

most commonly brain or lung. As already stated, it is probably an enzyme, requiring ionized calcium salts as its co-factor. An increase in the stability of the blood platelets, or a reduction in their number, would evidently delay coagulation of the blood. It is now thought that the former factor is responsible for the extremely delayed clotting which occurs in hæmophilia. Again, deficiency in the number of the platelets may lead to the occurrence of purpura. It is believed that normally the platelets have the function of protecting the walls of the capillaries, so that in their absence, relative or complete, defects in these walls are liable to occur, with consequent bleeding into the tissues. It is by no means certain that all cases of purpura are due to deficiency in the number of platelets in the blood, but it has been observed that in some cases of toxic purpura, e.g., those sometimes following the administration of sedormid (allyl-isopropyl-acetylurea), there is a very marked decrease in the platelet count. Again, it has been found possible to produce an antiplatelet serum, and injection of this into animals has caused a condition resembling purpura hæmorrhagica.

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Many other substances are known which possess the power of neutralizing the action of thrombin. Bleeding continues from the incision made by the medicinal leech for some time after the animal has been removed, and from the buccal glands of that animal a powerful anticoagulant, *hirudin*, has been prepared commercially. It acts both *in vitro* and *in vivo*, and that it is an antithrombin is shown by the fact that if an excess of thrombin be added to hirudinized blood, clotting takes place very rapidly. It has been extensively employed in laboratory experimental work to prevent clotting in animals, but does not seem to have been used clinically. Some of the azo-dyes, e.g. Chicago blue 6B, and chlorazol fast pink B.K.S., are powerful anticoagulants, both *in vivo* and *in vitro*, probably acting also by neutralizing thrombin. As they are relatively non-toxic, they are often employed in laboratory work, but again have not been used clinically.

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is heparin, first obtained in an impure state from liver by Maclean in 1916. Later, Howell and Holt worked on extracts of dog liver and gave their still impure substance this name. It is now prepared chiefly from ox liver, although lungs, intestinal wall, and striated muscle also contain fair quantities. There is good reason to believe that it is formed in the tissue mast cells, but it is thought that the natural antithrombin of blood is not in fact heparin.

The activity of any sample of heparin is best defined in terms of "units". The original "unit", that of Howell, represented the degree of activity which would prevent the clotting of 1 c.cm. of cat's blood kept in the cold for twenty-four hours. Since then, however, a crystalline barium salt of heparin has been prepared, and as the clotting power of cat's blood may vary from animal to animal it is better to employ this pure substance as a standard. The "unit" is now defined as the amount of anticoagulant activity contained in 0.01 mgm. of the standard. This unit is equivalent to about five of the old "cat units".

The production of anaphylactic shock or the injection of peptone in animals is followed by a marked decrease in the coagulability of the blood. It has been found that salmine, one of the protamine class of proteins, will combine with heparin to form a substance devoid of anticoagulant activity. It is thus possible to determine the amount of heparin present in a sample of plasma by finding how much salmine must be added to the plasma to give the shortest coagulation time. By means of this method, it has been shown that the incoagulability of the blood in peptone or anaphylactic shock is due to a great increase in the heparin content of the blood, due to its release from the liver. It is a curious fact that when heparin is added *in vitro* to a mixture of pure constituents—fibrinogen, prothrombin, and thrombin—there is no delay in clotting. It is believed that the albumin fraction of the blood is a necessary co-factor in its action.

Heparin possesses another property in relation to the clotting of the blood, in that it antagonizes the action of thrombokinase. A similar power is possessed by the venoms of certain snakes, notably that of the cobra, *N. tripudians*, but also as a rule of those of other members of the *Colubridæ*. On the other hand, venoms obtained from the *Viperidæ* in general but especially from Russell's viper, *V. Russellii*, resemble in action thrombokinase. One of the causes of death from viper bites is a massive intravascular thrombosis. Advantage has been taken of this property, and a dilute solution, 1 in 10,000, of Russell's viper venom, has been applied successfully to local bleeding in cases of hæmophilia, in which condition, as already stated, there is a deficiency of thrombokinase.

Any substance which can remove calcium ions from the blood, either by precipitating them in an insoluble form or by forming with them an un-ionized complex, will delay clotting, and the laboratory use of oxalates, fluorides, and citrates *in vitro* is based on this fact. The poisonous properties of the first and second of these preclude their use in clinical work, but citrates have been employed in blood transfusion, the donor's blood being

received directly into an isotonic solution, 3.8 per cent., of the sodium salt.

Dicoumarol.—Investigation of a hæmorrhagic disease in livestock in the U.S.A. led to the isolation by Link and his colleagues of a coumarin derivative, 3:3'-methylene-bis-(4-hydroxycoumarin) from "spoiled" sweet clover hay, which had been used as a feeding stuff. It has the property, when given in adequate dosage, of depressing, in animals and in man, the level of prothrombin in the blood. It acts apparently by affecting the liver but it does not seem that that organ is seriously damaged by the drug, although there is one report of liver necrosis having occurred in dogs. Renal changes have, however, been described, although rarely serious. Small doses are said to raise, and large to reduce, the fibrinogen content of the plasma, acting again on the liver and in a manner which has been described with other substances affecting that organ.

The drug is now prepared synthetically, and marketed under the name "dicoumarol". It has the advantage over heparin of being much less expensive. On the other hand, unlike heparin, its action is slow in onset, but when established is rather prolonged. Again, the drug is somewhat variable in its intensity of action, even from day to day in the same patient, so that it is not possible to lay down any dosage as appropriate for repeated administration.

Reduction of the prothrombin level in the blood should lead to delay in clotting of the blood. In fact, however, the amount normally present there is considerably in excess of the minimum concentration required, so that until the level has been reduced to about 30 per cent. of the normal the coagulation time is not greatly lengthened. Owing to the variations in activity which occur or may occur in any one patient on a steady maintenance dose of dicoumarol, it is most necessary that daily prothrombin estimations should be made. If this is not done, there may be a fall in the blood level even to zero, and consequently severe hæmorrhages may occur. Should the prothrombin level fall dangerously low, blood transfusion is the best remedy, but as prothrombin tends to disappear from blood kept *in vitro* for transfusion purposes it is advisable to obtain fresh blood for any case. Vitamin K, or its substitutes, might seem to be the proper remedy but time is required for their action, and there is no time to spare; none the less, menaphthone should be given, together with the transfusion, but the latter is the more urgent requirement.

ANTICOAGULANTS IN CLINICAL PRACTICE

Both heparin and dicoumarol have been employed extensively in a wide range of conditions, to prevent the occurrence, or to limit the extension, of thrombosis. Thus, heparin has been used in cases needing arterial suture or venous grafts to prevent the formation of thrombi at the points of injury of the vessel wall. Similarly, it has been used to prevent extension of a thrombosis in thrombophlebitis and similar conditions, in pulmonary em-

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duction of heparin, whilst others have used dicoumarol with very good results.

There are then these two powerful and valuable drugs available in this condition, and it remains to choose between them.

The choice of drug.—To aid in the choice it will be well to consider each from several aspects, the speed, duration, and constancy of action, the risk of toxic effects, and, of least importance, the cost. As to the last of these there is no question, dicoumarol being very much cheaper than heparin. Intravenous injection of heparin produces a very rapid action, within about ten minutes, but it is much less reliable on subcutaneous injection, and useless by mouth. Intramuscular injection is reliable and gives a fairly rapid action. Dicoumarol, however, is effective either by mouth or parenterally, but is slow in action, the prothrombin level being reduced only after the lapse of from twenty-four to seventy-two hours. When speed of action is wanted, and this is often the case, heparin should evidently be preferred, although some authors advise its discontinuance when the action of dicoumarol, given from the start, has shown itself. The duration of action of heparin is low, the effect of a single dose of 6000 units passing off in about three hours. The dose can, however, be repeated as needed, or an intravenous drip may be instituted, by means of which the coagulability of the blood has been maintained at a low level for a matter of weeks. The rate of drip should be varied in accordance with the changes in the coagulation time, determined preferably at least daily, but as an initial figure some 10 to 20 units per minute may be suitable. The duration of action of dicoumarol, when established, is great, as even after the cessation of all treatment the liver takes some little time to raise the prothrombin in the blood to the normal level. It might be thought therefore that it should be the drug of choice on these grounds, as repeated injections or an intravenous drip are procedures to be avoided when possible. One of its great disadvantages, however, is its inconstancy of action, not only from patient to patient, which might be tolerable, but also in the same patient from day to day. There may be great variations with no warning in the prothrombin level, and this really confines its use to institutions where this level can be determined daily, and practically excludes its use by the general practitioner. The determination of the coagulation time of the blood is a more simple procedure, and this is all that is usually required when heparin is being used. In this respect then heparin is preferable to dicoumarol. Considering now the question of toxicity and its necessary corollary, the alleviation of any untoward effects, both drugs cause the same effect, the production of hæmorrhage, and deaths have occurred following the use of both. It is, however, very much easier to combat the effects of an excess of heparin than those of dicoumarol. Heparin being neutralized in its action by protamines, the injection of salmine sulphate solution will as a rule restore the coagulability of the blood. On the other hand, to antagonize the effects of dicoumarol the transfusion of a large volume of fresh blood or plasma will be needed, and this will probably have

bolism and, though it seems rarely only, in coronary thrombosis. It has also been employed to prevent fibrin formation, and consequently adhesions, in cases of pleural effusion, and has been administered intrathecally in cases of meningitis with the same object. At one time it had a considerable vogue, especially in the U.S.A., in conjunction with sulphathiazole, in the treatment of subacute bacterial endocarditis, to limit the further deposition of fibrin on the damaged valve surfaces; but this procedure seems to have been a failure. In a similar range of conditions dicoumarol has also been employed, and often with success. Like heparin, it has failed in the treatment of subacute bacterial endocarditis.

A somewhat unexpected result has been obtained with both drugs in the treatment of *thrombosis of the retinal veins*. The drugs must be used in the early stages of the condition, for if delayed beyond this no benefit is likely to occur. A rational explanation is not easy to find, but it may be that although thrombosis has started in one or more of the veins, it is not complete, so as to block the lumen of all of them. By reducing the coagulability of the blood, the extension of the process may be stopped, so that at least some of the veins remain patent.

Apart from such a relatively rare procedure as actual surgical interference with the vessel wall, there are two conditions in which anticoagulant drugs might seem called for:—venous thrombosis, usually in the leg veins, with the concomitant risks of pulmonary embolism and coronary occlusion.

The primary cause of *venous thrombosis* is still not clearly decided. Bacterial infection has often been blamed and sometimes doubtless rightly. As, however, the condition is at least as common to-day, with more rigid aseptic technique, as it was in the past with less careful asepsis, it seems difficult to accept infection as the sole, or even as the most common cause. Again, as Bauer has recently pointed out, venous thrombosis occurs quite often, although not always diagnosed, in medical wards where bacterial infection can hardly be blamed. No doubt, slowing of the rate of flow of blood through the veins is one of the causes, but whether this alone, in the absence of damage to the vessel wall itself, is sufficient, is still open to doubt. None the less, early movement in suitable postoperative cases is a valuable preventive of the condition, and here increased rate of blood flow in the veins may well be of the highest importance.

Bauer has pointed out that venous thrombosis is still a relatively frequent event. He cites figures of surgical cases from Europe to show that in nearly 180,000 cases it occurred in almost 3000, with about one-sixth dying from pulmonary embolism. The figures of case incidence and of mortality following labour were much lower, but he argues that they are an underestimate, as often the women left hospital too early for thrombosis to have shown itself. An approximate incidence of 2 per cent., with one-fifth dying from pulmonary embolism, is given for medical cases. He insists on the necessity of early diagnosis of the condition and describes certain physical signs and symptoms which point to the existence of a beginning thrombosis in the veins, usually of the lower leg, and in doubtful cases he advises phlebography with a contrast medium. His own figures show a striking difference after the intro-

REVISION CORNER

THE DIAGNOSIS, TREATMENT, AND PREVENTION OF NAPKIN ERUPTIONS

THE most common type of napkin eruption is a contact dermatitis, the result of alkalis or irritating soap residues in napkins or of free ammonia produced by decomposition of urea in the urine by organisms in the stools. These inflammatory reactions are often termed *napkin erythemas* and Jacquet described them as "dermites infantiles simples". He classed them into four types of lesion: (1) simple erythemas; (2) vesicular erythemas; (3) erythematous papules; (4) small ulcerations. It is obvious that the type of lesion will depend upon the potency of the irritant and the degree of secondary infection and not least upon the general condition of the patient. When a napkin dermatitis is severe and persistent a secondary eczema may develop and become apparent by grouped weeping papulo-vesicles. A general sensitization by autolytic products may often become manifest by an eruption of red macules or eczematous areas upon the body and occasionally upon the limbs. These secondary eruptions require a cooling lotion or a soothing cream, such as 2 per cent. ichthammol in calamine oil lotion. If the primary napkin dermatitis is soon controlled the secondary eruption will disappear.

Contact dermatitis usually affects the convex surfaces which are naturally in closest contact with the napkin, whereas *intertrigo* affects the folds and produces a bright red surface which may exude. Although the term *intertrigo* is sometimes reserved for a dermatitis produced by moisture and friction between the opposing layers of skin, it may usefully be classified as (1) *simple*, when the above factors alone are concerned; (2) *pyogenic*, when pus-cocci produce erosions or small ulcers between folds of skin; (3) *seborrhæic*, when it shows the scaly type of mild dermatitis apt to involve many flexures of the body and to be associated with a scurfy scalp; and (4) *mycotic*, when due to yeasts, or much more rarely to ringworm.

PREVENTION

Prevention of these eruptions depends upon careful attention to the hygiene of the infant. Napkins should not be washed with common soap-flakes containing excess of alkali nor with strong soaps; they should be well rinsed in two or three changes of water and thoroughly dried. If there is any tendency for the infant to produce ammonia in the urine, the clean diapers should be wrung out, before drying, in saturated boracic acid solution or in 1:4000 perchloride of mercury solution. Small doses of grey powder may inhibit the intestinal bacteria and make the motions less irritating. When the infants are bathed, attention should be paid to the creases and folds of the skin, which should be washed clean and thoroughly dried and then well powdered with a bland dusting powder. Although the common proprietary powders are often satisfactory the following is particularly useful as an astringent and prophylactic against infection:—

R Powdered calomel	5%
Bismuth subgallate	45%
Zinc oxide or talc	to 100

TREATMENT

The prophylactic measures mentioned above will get rid of the external irritant which is the most common cause of dermatitis of the buttocks and thighs. When the skin is inflamed, and especially if the surfaces are moist, normal saline or 1 per cent. sodium sulphate should invariably be used for cleansing the skin. Subsequently, it is often sufficient to apply a simple calamine lotion, but if secondary infection is present 1:1000 mercury perchloride or 3 per cent. solution of coal tar may be added to the lotion. The skin may be protected from infection and made more resistant

to be repeated before the liver has recovered from the effects of the drug sufficiently to produce prothrombin in adequate amounts. Vitamin K should be given too, but it also will be slow in producing its effects. On all grounds then, except that of cost, it seems that heparin is to be preferred to dicoumarol in cases of venous thrombosis. It may be noted that it is generally regarded as undesirable to administer either drug as a prophylactic measure before surgical operations. They should also be avoided in cases which show active ulcerative processes.

In a fair proportion of cases, even acute massive *pulmonary embolism* is not immediately fatal, a period of up to two hours elapsing before death occurs. In these, it is probable that the artery, originally partly blocked by the detached thrombus, becomes completely filled by an extension of the thrombotic process from the clot. The action of dicoumarol is far too slow in its appearance for it to be of the slightest value in these cases, but heparin has been used in large doses with success, the patient, curiously enough, making a complete recovery with no permanent ill-effects from the embolism.

From the available literature it does not seem that either drug has been widely used in cases of *coronary occlusion*, and the question of their value seems to be still a matter of doubt. There are some favourable reports of their action in such cases, chiefly with dicoumarol. In the acute fulminating case it seems unlikely that either drug would be of use, but in the frequent cases in which the patient recovers from the immediate effects of the occlusion their use might well be justified. In these cases the vessel walls throughout the heart are generally atheromatous and therefore predispose to the process of thrombosis. It seems not possible to suggest that either heparin or dicoumarol should be administered for years to prevent a further attack of occlusion. On the other hand, there are many anastomotic channels between the two coronary arteries, and it seems that the use of an anticoagulant might delay the extension of the thrombosis from the site of the occlusion, and so permit these anastomotic channels to widen and thus supply the ischæmic part of the heart with more blood, so limiting the effect of the occlusion. On the whole, the use of dicoumarol might prove preferable to that of heparin in these cases, owing to its longer lasting action, but an initial administration of heparin seems advisable, to prevent any immediate extension of the thrombotic process. It may be argued that the use of these drugs will prevent the formation of the mural thrombus which, no doubt, helps to strengthen the damaged heart wall, but there is every reason to believe that this will occur after the cessation of treatment with the anticoagulant. The whole question of the use of the drugs in coronary occlusion must, however, be regarded as still *sub judice*, until more reports of their use have appeared.

the immediate and remote prognosis is less favourable than after a vaginal delivery. The immediate mortality of "clean" cases in expert hands is 0.5 to 1 per cent. The average mortality in hospital statistics is 2.5 per cent., this higher figure being due to the more serious types of cases admitted to hospital. The average maternal mortality over the country is believed to be nearer 10 per cent. than 1 per cent., owing to the unjustifiable risks sometimes taken in unsuitable surroundings. The remote disadvantages of the operation are the prolonged convalescence and the considerable time which must pass before the woman can resume her normal duties, the frequent occurrence of abdominal pain and discomfort, the lowered fertility rate, and the risk of rupture of the uterus in a subsequent pregnancy.

An argument put forward for the wider use of Cæsarean section is that thereby foetal life is preserved. This is only partly true, as the stillbirth and neonatal death rate is not negligible. It is well known that the average baby born by Cæsarean section does not breathe as spontaneously or as quickly as a baby delivered by the vagina. The reason for this is not known, but it has been suggested that the squeezing action on the lungs and head produced by the passage through the birth canal is probably a major stimulus to respiration. The death rate varies with the condition for which the operation is done, and also with the anæsthetic used, as well as with the experience of the anæsthetist. In Marshall's series of 246 consecutive cases, in which there was a variety of indications and only local anæsthesia was used, the stillbirth and neonatal mortality was 4.7 per cent. In Munro-Kerr's series of 301 cases of contracted pelvis it was 3.8 per cent. This latter figure, however, compares very favourably with the foetal mortality of 19.2 per cent. in a series of cases of trial labour for contracted pelvis.

INDICATIONS

Contracted pelvis is an unquestionable indication when it is of a severe degree or when there is serious disproportion between the size of the foetal head and the maternal pelvis. A true conjugate of less than 7.5 cm. or an antero-posterior diameter of the outlet of less than 10 cm. is an absolute indication. With a lesser degree of pelvic contraction an elective Cæsarean section may be considered advisable (a) when the patient is an elderly primigravida and the high value of the foetus makes a trial of labour unjustifiable; (b) when the patient has had an unsuccessful trial of labour in a previous pregnancy with the birth of a stillborn or damaged baby; (c) when, in addition to pelvic contraction, there is a breech presentation.

An X-ray pelvimetry should be obtained in every case of contracted pelvis so that the degree, position and extent of the contraction can be accurately seen and, in addition, the size of the foetal head in relation to the size of the pelvic cavity determined. In the use of this method of diagnosis considerable experience is required. A careful clinical examination of the pelvis, if necessary under anæsthesia, should be carried out and the degree of disproportion estimated by Munro-Kerr's modifications of Müller's method. In the borderline case, when there is some uncertainty whether or not the head will pass through the pelvis, trial of labour is the best method of treatment, especially in the young primigravida.

Pelvic tumours.—A fibroid on the cervix or lower pole of the uterus which fills the pelvic cavity is an indication which no one will dispute. Most obstetricians would agree that an ovarian cyst in the pelvis is an indication, but some advocate removal of the cyst, even although labour is imminent, followed by a vaginal delivery. Carcinoma of the cervix is an absolute indication as it is inadvisable to allow the cervix to be dilated.

Vaginal conditions.—Cicatrical contractions of the cervix or vagina are usually an indication. Previous plastic repair operations of urinary or rectal fistulæ, particularly when more than one attempt at repair has been done, are definite indications. Previous plastic repair operations, e.g., for prolapse, are not absolute indica-

by applying a lotion of boracic acid, 5 grains (0.32 gm.), tannic acid, 20 grains (1.3 gm.), camphor water to 1 ounce (28.4 c.cm.), and this may be preceded by painting with 1:1000 proflavine solution in water. If the skin becomes dry and cracks, zinc and yellow mercuric oxide paste may be smeared lightly over the dried surface the last thing at night. It is undesirable to keep the napkin area constantly under greasy applications but emollient creams are useful in certain phases.

Intertrigo will respond to similar measures, the pyogenic type calling for the antiseptic dyes and the seborrhœic type for calamine lotion plus 2 per cent. of precipitated sulphur. Yeast infection of the perianal area is a somewhat rare complication of thrush, and the skin lesions will clear quickly with the antiseptic lotion mentioned. Recovery is assisted in all these eruptions by exposing the naked skin to dry, warm air for a short period after the bath. Waterproof drawers should be reserved for rare social occasions.

CONGENITAL SYPHILIS

Consideration of the erythematous eruptions in the napkin area must also include congenital syphilis. In this case the lesions are of a deeper hue, the redness having a brownish or lilac tint, often described as "hammy". The individual lesions are sometimes smaller than those of a contact dermatitis, and similar lesions may be seen upon the limbs, palms and soles. The liver and spleen are often enlarged, and if the infection is severe the infant will be wizened, have snuffles, and may show areas of osteochondritis or periostitis on X-ray examination of the long bones. The disease, fortunately, is still uncommon, but about half a dozen cases have been seen at the Hospital for Sick Children in the last two years. Confirmation of the diagnosis can usually be obtained by the Wassermann reaction of the infant and the parents.

R. T. BRAIN, M.D., F.R.C.P.

INDICATIONS FOR CÆSAREAN SECTION

CÆSAREAN section has probably given rise to more discussion than any other subject connected with midwifery, and there is still difference of opinion as to the limits of and indications for the operation. The early history of the operation is not known, but we know that it was practised by the Greeks after the death of the mother. The oldest authentic record, 408 B.C., of a living child born by means of the operation is that of Gorgias, a celebrated orator of Sicily. The operation on the living is of more recent date but its beginnings are also lost in antiquity. It is mentioned in the *Mishnagoth*, the oldest book of the Jews, published in 140 B.C. The first Cæsarean section in Great Britain was performed in 1737 by Mr. Smith, an Edinburgh surgeon, on a patient who had been in labour for six days. The first successful Cæsarean section in Great Britain was performed by a midwife, Mary Donally, in 1738, on a patient who had been in labour for ten days. During the last sixty years the scope of the operation has increased and it has changed from a last-minute attempt to remove a living fœtus from a moribund woman to a planned operation at a selected time in pregnancy.

The number of conditions in which the operation is indicated is large, but with few exceptions none is absolute and each individual case has to be assessed on its merits, taking into account such factors as age, parity, relative fertility, state of health, relative size of the pelvis and fœtus, as well as the presentation of the fœtus. When considering the use of Cæsarean section it should be kept in mind that the aim of the care of the pregnant woman is to ensure delivery of a healthy baby and an undamaged mother, with her complete restoration to health after confinement. When properly indicated the operation is a life-saving measure for both mother and child, but it is neither the safe nor simple procedure for either mother or child that it is popularly believed to be. Statistics have repeatedly and consistently shown that

the immediate and remote prognosis is less favourable than after a vaginal delivery. The immediate mortality of "clean" cases in expert hands is 0.5 to 1 per cent. The average mortality in hospital statistics is 2.5 per cent., this higher figure being due to the more serious types of cases admitted to hospital. The average maternal mortality over the country is believed to be nearer 10 per cent. than 1 per cent., owing to the unjustifiable risks sometimes taken in unsuitable surroundings. The remote disadvantages of the operation are the prolonged convalescence and the considerable time which must pass before the woman can resume her normal duties, the frequent occurrence of abdominal pain and discomfort, the lowered fertility rate, and the risk of rupture of the uterus in a subsequent pregnancy.

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tions, but since there is a high recurrence rate of prolapse after a carefully conducted vaginal delivery with episiotomy the operation is advisable.

Placenta prævia.—When the placenta completely covers the internal os, Cæsarean section gives the best results for the mother and child. It is also the method of choice when the placenta is situated on the posterior wall and reaches, but does not overlap, the internal os, and also in cases of placenta prævia in which the cervix is long and hard and barely admits one finger. Macafee has reported a maternal mortality of 0.57 per cent. and foetal mortality of 23.5 per cent. in a series of 174 cases with this line of treatment. These results compare favourably with the returns from 11 teaching hospitals in Britain where 3,103 cases of placenta prævia were treated by various methods with a maternal mortality of 5.9 per cent. and a foetal mortality of 54 per cent.

Accidental hæmorrhage.—The rare cases of concealed hæmorrhage in which bleeding into the uterine cavity is either marked or continuous require Cæsarean section with, in addition, sometimes hysterectomy. The risk in these cases is extensive hæmorrhage between the muscle fibres of the uterus with loss of the function of contraction and retraction.

Pre-eclamptic toxæmia.—There are two groups of cases in which the operation should be considered: (1) Patients with severe pre-eclampsia (blood pressure over 170 mm. Hg systolic, with albuminuria, and with or without œdema) who fail to respond to adequate medical treatment in twenty-four to forty-eight hours, particularly when in addition they complain of severe frontal headache, visual disturbance, epigastric pain or vomiting; (2) patients with a less severe degree of toxæmia, to whom prolonged treatment has been given but who, after a period of improvement, show a rise in blood pressure, with marked œdema and increased albuminuria. The risk of eclampsia supervening in these two groups is considerable, but the decision to perform a Cæsarean section will depend also upon the parity of the patient, the duration of the pregnancy, whether the fœtus is alive or not, and the condition of the cervix.

Eclampsia.—Surgical treatment of eclampsia was common about thirty years ago but the high maternal mortality led to its general condemnation. There are still two groups of cases in which it is justifiable:—(1) in cases of ante-partum eclampsia in primigravida who have failed to go into labour four to five days after the last fit; (2) the rare case of fulminating eclampsia in which fits recur at frequent intervals in spite of efficient and adequate treatment.

Hypertension complicating pregnancy. It is well known that the foetal mortality is high when the blood pressure is over 160 mm. Hg from early in pregnancy. The risk of intra-uterine death of the fœtus in the last month is so great that operative interference is justifiable.

Chronic glomerular nephritis.—The risk of intra-uterine death is high in this condition owing to infarction of the placenta. Cæsarean section should be carried out not later than the 36th week, particularly in cases in which the fœtus has ceased to grow.

Heart disease, diabetes, and rhesus incompatibility.—These conditions are often given as indications for operation. Heart disease alone is rarely an indication and statistics show that the immediate and remote results of vaginal delivery are better than those of Cæsarean section. In diabetes and rhesus incompatibility the foetal mortality is about the same with induction as with operation, and as the section is done in the interests of the child there is no justification for its use.

Obstetrical complications which may lead to an antenatal decision to do a Cæsarean section are (1) breech presentation in an elderly primigravida or in a patient of low fertility; (2) persistent abnormal presentation, e.g. breech or shoulder, in a primigravida with no obvious cause; (3) previous Cæsarean section when the condition for which it was indicated is still present or when the previous section had

been complicated by sepsis, particularly if the operation had been a classical one.

During labour.—The operation may be indicated (1) when the umbilical cord prolapses at an early stage in labour with the head still high and the foetal heart still beating; (2) in cases of uterine inertia when, in spite of many hours or days in labour, the cervix either does not dilate or dilates only to a slight degree; (3) in cases of contraction ring in the first stage of labour, rarely in the second stage; (4) in cases of trial labour when the head does not descend in spite of good pains, or when maternal or foetal distress occurs in the first stage of labour; (5) in cases of breech presentation when in spite of good pains the breech does not descend into the pelvic cavity; (6) in cases of pregnancy in one horn of a bicornuate uterus when the non-pregnant horn obstructs the descent of the presenting part; (7) in the rare cases of sacculatation of the uterus.

GLADYS H. DODDS, M.D., F.R.C.S., F.R.C.O.G.

THE TREATMENT OF HÆMORRHOIDS

HÆMORRHOIDS are external or internal according to their anatomical origin. The external type arise in the lower half of the anal canal and in the region of the mucocutaneous junction. They are lined with squamous epithelium and, in contrast to internal hæmorrhoids, are well supplied with sensory nerve endings. External hæmorrhoids comprise two main types: the acutely occurring anal hæmatoma, incorrectly designated a mucous or thrombotic pile because the extravasated blood clot is always outside the vein, and the chronic fibrous ridges and external tags which are essentially œdematous infected rugæ. Internal hæmorrhoids arise in the lower inch of the rectum and upper part of the anal canal, and consist chiefly of tortuous and dilated veins accompanying the terminal branches of the superior hæmorrhoidal artery. They have a covering of columnar epithelium and are insensitive. Three grades are recognized: the primary or first degree, in which the pile reaches but does not extend beyond the anal orifice; the intermediate or second degree, in which protrusion may occur beyond the sphincter but reduction is spontaneous as soon as the expulsive effort of defæcation ceases; and the final or third degree, in which protrusion is marked and manual reduction becomes necessary.

Treatment entails careful and accurate examination to obtain correct diagnosis of the type of hæmorrhoid and to exclude associated pathology. A synopsis of diagnosis is given of a review of 163 cases of "piles" and "hæmorrhoids" referred during the past two years to a general surgical out-patient department:—

Internal 98 (first degree 33 per cent, second degree 45 per cent., third degree 22 per cent.); external 41 (anal hæmatoma 21, tags 20); fissures 19; pruritus ani 10; perianal abscess 4; polypi 3 (of which one was malignant); fistulæ 2, and condylomas, anal warts and colitis, one each.

INTERNAL HÆMORRHOIDS

The treatment of internal hæmorrhoids is palliative, by injection, or operative according to their degree or local condition.

Palliation is indicated for the constipated patient—more often female, with rectal congestion due to excessive and irritant aperients and careless bowel habits. The pregnant woman with temporary venous congestion and the plethoric male with chronic cirrhotic liver also come into this group. Treatment is on medical lines with a high-fluid, low-residue diet, avoiding stimulants, such as alcohol, and irritants such as curries and spices. The bowel is regulated with a bland aperient, such as extract of cascara sagrada, liquid extract of malt and liquid paraffin, of each one ounce (28.4 c.cm.), with an initial dose of 120 minims (6.12 c.cm.), later reduced to 60 minims (3.6 c.cm.) daily, as normal bowel habit returns. When anal tenderness is present, local application of equal parts of zinc and castor oil ointment will prove beneficial. Palliative treatment is reserved also, in the initial stages, for prolapsed thrombosed piles when œdema and congestion, and probably local sepsis, are

present. Reduction into the rectum is effected, with an anæsthetic if necessary to stretch the sphincter when unduly tight, and the pile masses are retained in position by cold compresses and elevation of the foot of the bed. Operation is carried out later.

Injection therapy, with 5 per cent. phenol in olive oil, and menthol 2 grains per oz. (0.13 gm. per 28.4 c.cm.) is most suitable for first and second degree hæmorrhoids, and is unlikely to succeed when there is a history of prolapse or when bleeding is present at times other than following defæcation. Sixty-one per cent. of the total of 98 patients with internal hæmorrhoids were so treated, the group including all of the first and 58 per cent. of second degree. Internal primary hæmorrhoids present, as a rule, in the anatomical (lithotomy) situation of 3, 7 and 11 o'clock, with occasional secondary masses at 2, 5, 6 or 9. The quadrant chosen for injection is that which presents the largest pile, but two or three injections of 3 to 4 c.cm. each of phenol solution can be given at one treatment. The actual injection is made submucously into the pedicle of the pile. Thus, if the Thames represents the anal canal and Southend the pile, the injection would be in the region of Leigh-on-Sea. With correct technique the patient should not experience any pain, for the anal mucosa is insensitive, and if pain is felt, the injection is placed too low down.

Operative treatment is reserved for third degree hæmorrhoids when protrusion is uncontrollable, and for copious and recurring bleeding which has not responded to earlier injection therapy. In the present series, 42 per cent. of second degree and 87 per cent. of third degree hæmorrhoids were so treated. Careful preparation is essential, extending over two clear days before operation. On the first day an aperient is given, graded according to the patient's habits. Thus, for the patient who does not indulge in aperients, 60 minims (3.6 c.cm.) of cascara evacuant may suffice, whereas for the confirmed purger, one ounce (28.4 c.cm.) of castor oil may be necessary. The diet is a fluid low-residue one, avoiding roughage. A soap and water enema is given on the night preceding operation, followed by a rectal washout on the following morning. Nephenthe, 10 minims (0.6 c.cm.) t.d.s., is given after the initial enema, and continued for two days following operation. It allays postoperative discomfort and maintains an action-free bowel for the first three postoperative days. Details of operative technique are well described by Milligan (1937). Following operation a tube of approximately 12 mm. external diameter, encased in a tulle gras dressing, is inserted into the rectum and retained for forty-eight hours. A mild aperient is given on the third day, followed by an olive oil enema on the following morning. Baths are also begun on the fourth postoperative morning, digital dilatation of the rectum on the sixth, and the patient is instructed in the art of inserting a finger into his rectum on alternate days while in his bath for two or three weeks, in order to ensure absence of postoperative stricture.

EXTERNAL HÆMORRHOIDS

The treatment of anal hæmatoma depends upon the stage at which the patient presents himself. In the acute stage, excision of the hæmatoma under local anæsthesia is the method of choice. The clot is evacuated through a wedge-shaped incision with the apex medially. Palliative treatment is advised for the hæmatoma which has passed the acute stage and is beginning to subside. In the series dealt with, roughly half were operated upon. Chronic external fibrous skin tags are also dealt with under local anæsthesia by similar wedge-shaped excision. For both types of external hæmorrhoid local comfort is greatly enhanced by the injection of 5 c.cm. proctocaine on each side of the sphincter.

WILLIAM MICHIE, M.B., F.R.C.S.ED.

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NOTES AND QUERIES

Anæsthesia for Midwifery in Country Practice

QUERY.—Anæsthesia for midwifery in a country district cannot involve bulky apparatus that might have to be carried across fields at night. At present I leave a quick-acting barbiturate with the mother, to take early in labour, give pethidine later, and use chloroform to complete the second stage. Is it safe to add one of the small trilene-and-air analgesia apparatuses now on the market to this pharmacological pot-pourri; either to precede or, if sufficient, to replace the chloroform anæsthesia?

REPLY.—Trichlorethylene (trilene) is a quick-acting and effective analgesic drug which is non-inflammable, and for this reason is a valuable alternative agent to chloroform in domiciliary obstetric practice. Marrett has designed a useful apparatus which enables air to be drawn over trilene so that analgesia is easily and speedily produced and may be deepened into anæsthesia towards the end of the second stage of labour. This apparatus is portable, economical in use, and may be purchased at a reasonable price. Freedman's bottle is an excellent device for self-administered analgesia with trilene (0.65 per cent.) and air. In my opinion it would be safe to include either of these apparatuses in the "pot-pourri" described in the query, and for general utility the former is preferable as it provides both analgesia and anæsthesia.

ARCHIBALD MARSTON, M.R.C.S., D.A.

Dextro-amphetamine Sulphate (Dexedrine) in Obesity

QUERY.—I shall be glad of information on the toxicity of dextro-amphetamine sulphate (dexedrine) used for the purpose of weight reduction.

REPLY.—Dextro-amphetamine (dexedrine) and its optimal isomer amphetamine B.P. possess very similar properties, subject to certain quantitative differences. Both drugs are powerful excitants of the brain and, in addition, provoke the peripheral effects of sympathetic stimulation. With dextro-amphetamine the cerebral effect overshadows the sympathetic more completely than is the case with amphetamine B.P. Consequently, when used in the treatment of obesity, for their action on the brain, dextro-amphetamine is less likely than the official drug to excite undesirable sympathetic side-reactions. The symptoms of gross overdosage may be distressing and even dangerous, and sometimes occur in hypersusceptible subjects even after conventional doses. The risk of such idiosyncratic response can be minimized by making the

initial dose a very small one. Hypersusceptibility develops after one or two standard doses.

Colton (1943) and his fellow workers clarified the dosage problem by personally taking amounts up to 100 mgm. of dextro-amphetamine in seventy-two hours and concluded that 60 mgm. to 80 mgm. per forty-eight hours could safely be given without causing distress. Cases should nevertheless be selected with discretion and patients with psychopathic personalities, hypertension, advanced arteriosclerosis or coronary artery disease, carefully excluded.

Instances of acquired tolerance have been described, enforcing the use of increasing doses, but a short period of abstinence quickly restores responsiveness to the original dose of drug. Addiction, too, may occur but Finch (1947) reassuringly reports on 400 cases that, if the withdrawal period be spread over a period of two or three weeks, the habit can consistently be broken.

NATHAN MUTCH, M.D., F.R.C.P.

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Gastric Secretion Tests

QUERY.—Can you give me any information on (1) nocturnal test meals, and (2) differential measurement of gastric and duodenal pH? I would like to know the fallacies and technique of these tests, the normal ranges of results, and their value in diagnosis and treatment.

REPLY.—(1) *Nocturnal secretion tests*.—Gastric night secretion investigations are being employed by some in the belief that the acid secreted during the night is an important etiological factor in duodenal ulcer, since at that time the protective buffering action of food is lacking. No stimulus is used, as it is the spontaneous secretion which is being assessed. I use the following technique:—

The patient is allowed a full gastric diet, but after the evening meal at about 6.30 p.m. nothing further is given. Smoking and all drugs are forbidden. At 9.30 p.m. a Ryle's tube is swallowed and the stomach is emptied as completely as possible. Continuous suction is then maintained until 9.30 a.m. by a method which allows hourly sampling as well as collection of the whole night secretion. The samples are titrated and plotted in the ordinary way. A sample of the whole mixed secretions is also titrated, its pH measured electrically, and the total volume noted. From these figures is calculated the total in grammes of HCl secreted throughout the night.

After employing this test over a hundred times I have come to the conclusion that it gives more dramatic evidence of abnormality than do test meals.

The levels of acidity found in duodenal ulcer patients are often well above those which follow histamine injection in the same patients, and 40 or 50 units of free HCl have been found in the spontaneous night secretion of several patients who were histamine-fast achlorhydrics. Volumes of 1000 c.cm. or more may also be noted, although in normal controls a volume of over 500 c.cm. has been rare and volumes of less than 100 c.cm. are common. It is not possible to define a normal range, but it seems clear that the average normal is well below t

average in cases of duodenal ulcer, both in volume and acidity. I estimate 0.5 gm. of HCl in the whole of the aspirated night secretion to be very roughly the upper limit of normality. No striking difference from normal has been observed in gastric ulcer patients.

I am critical of the value in diagnosis of all secretion investigations, since the laws which govern them are laws of averages only, and therefore inapplicable to individual cases. It is, however, reasonable to regard excessive night secretion as a reinforcing indication for the operation of vagotomy in a case of duodenal ulcer, for this procedure is known considerably to reduce secretion of acid at night (Dragstedt, 1945; Orr and Johnson, 1947). I would also regard such a finding as a contraindication to gastro-enterostomy.

The fallacies of test meals and secretion investigations are numerous, but mostly tend to lower the observed values. High levels may therefore still be regarded as abnormal. The questioner is referred to the work of Ihre (1938) and of Teorell (1935).

(2) *The differential measurement of gastric and duodenal pH.*—The technique of simultaneous duodenal and gastric intubation is difficult and time-consuming and could not be used routinely. Further, the electrical measurement of pH requires expensive apparatus and is unreliable unless skilfully carried out. Berk, Thomas and Rehffuss (1942) found evidence of a failure of adequate neutralization of acid in the duodenal bulbs of ulcer patients.

H. D. JOHNSON, F.R.C.S.

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Epidermophytosis

QUERY.—Could you advise me how to treat a case of active epidermophytosis, mainly of the palms of the hands, and slightly effecting the soles of the feet? It has been present for almost a year and has resisted the application of salicylic acid in methylated spirit, and zinc and salicylic acid powder. I have also tried mycil. X-ray treatment was given originally as the condition was thought to be cheiopompholyx.

REPLY.—The first consideration in a dermatologist's mind is that if epidermophytosis has been treated for a year and remains, then there is a high probability that the diagnosis was incorrect and that cheiopompholyx should be considered as an alternative. Such resistance to treatment and to a dose of X-rays is more characteristic of cheiopompholyx than of epidermophytosis. But, assuming the first diagnosis, then paint the feet three times with neat formalin solution, once every five days, using a

talc dusting powder night and morning between treatments. Follow this up with a 5 per cent. dithranol ointment for a week. Any reaction can be treated with castor oil ointment bandaged on twice a day. Throughout, the feet can be well washed with soap and water. If the condition persists the diagnosis should be reconsidered.

W. J. O'DONOVAN, O.B.E., M.D.

Enterospasm

QUERY.—"Intestinal Obstruction due to Paralytic Ileus due to Enterospasm." This is a copy from a death certificate issued in respect of a young patient of mine, after a post-mortem examination and an adjourned inquest, who died after being ill for only two days. It would seem that the remote or the real cause that led up to the fatal issue was "enterospasm", and I shall be grateful if you will inform me if this is a recognized disease entity. If so, what are its etiology, signs and symptoms? Would an irritant poison such as arsenic, or any other poison, produce spasm in the intestines and cause paralytic ileus and intestinal obstruction?

REPLY.—Enterospasm is a disturbance of function of the bowel which need not necessarily involve either disease or injury (by poison or otherwise) to the segment affected. It is a loose term unless applied in its strict physiological sense, and highly unlikely to cause serious obstruction, since it is spasmodic, intermittently obstructive, and not succeeded by ileus (as from fatigue). The only poison commonly causing enterospasm is inorganic lead (lead acetate, oleate or oxide). Death from chronic lead poisoning ensues from classical plumbism (anæmia, colic, blue line, neuritis, and possibly encephalopathy) and not from ileus and obstruction. It seems likely that some twisting, internal herniation or band obstruction of the bowel has been missed at autopsy.

KEITH SIMPSON, M.D.

Paludrine in Malaria in Children

QUERY (from India).—I shall be grateful if you will give me the dosage and contraindications to the use of paludrine in malaria in children.

REPLY.—In adults, an effective therapeutic dose of paludrine (0.3 gm. daily) does not produce any toxic effects. Doses of 1 gm. daily in some persons may cause vomiting, abdominal discomfort, and signs of renal irritation. Thus there is a safe interval between the therapeutic and toxic dose. Paludrine is not contraindicated in children, who may be given the same fraction of the adult dose as is given in treatment with quinine.

WILLIAM MACARTHUR, K.C.B., D.S.O., M.D.,

F.R.C.P.

PRACTICAL NOTES

Vagotomy in the Treatment of Peptic Ulcer

THE immediate and later effects of vagotomy in six cases of peptic ulcer are recorded by C. F. W. Illingworth and A. W. Kay (*Edinburgh Medical Journal*, October 1947, 54, 540). All the patients were men with duodenal ulcers, and in one case a gastric ulcer also; in all cases there was a long history of refractory indigestion with relapse after one or more periods of medical treatment in hospital; all were suffering at the time of operation from a severe and prolonged attack. Gastric motility and secretion were estimated before and after operation. In all cases the postoperative gastrograms showed almost complete immobility with only occasional slight alterations of tone. The effect of parasympathetic stimulation by intravenous injection of 0.5 mgm. prostigmin was noted in four cases: before operation it caused a distinct increase in gastric motility, but postoperatively was without effect. The immediate results of vagotomy were satisfactory in all cases, with complete relief of pain and indigestion. The relief, however, did not prove permanent: in one case, that with gastric as well as duodenal ulcer, there was relapse within three months, and further operation showed that the gastric ulcer had penetrated the pancreas. Two other patients required gastrectomy, having relapsed eighteen months and two years after vagotomy. A fourth patient relapsed after eighteen months. The remaining two remained symptom-free after three years. Motility records showed that in each case return of symptoms was preceded by return of motor activity and positive response to prostigmin, which suggested that the recurrence was due to regeneration of the cut nerves; in two cases this fact was confirmed by microscopic examination after gastrectomy. In conclusion it is stated that although the end-results appear poor, useful information was obtained: in five of the six cases there was prolonged healing of the ulcer, or prolonged relief of symptoms, following reduction of gastric motility, although the acid level remained unchanged. A like result may be obtained by the use of drugs such as atropine, and there would seem to be an indication for investigation of substances with similar action without harmful side-effects.

Thiouracil and Propylthiouracil in Thyrotoxicosis

A VALUATION of the antithyroid drugs thiouracil and propylthiouracil for the pre-surgical preparation of thyrotoxic patients and also for the

medical treatment of those in whom operation was not indicated has been carried out by R. C. Grauer, H. De Walt, and C. W. W. Elkin (*American Journal of the Medical Sciences*, January 1948, 215, 63) in a series of one hundred patients, 63 of whom received thiouracil and 37 propylthiouracil. The general procedure was as follows:—

Before institution of therapy a basal metabolism test, galactose thyroid function test, serum cholesterol determination and blood count were done on each patient. Throughout the course of treatment a white blood count and differential count were done weekly; basal metabolism test, galactose thyroid and serum cholesterol determinations two-weekly until maintenance dosage was established, and thereafter less frequently. During the first three months patients were examined at weekly intervals, then two-weekly for three months, and thereafter monthly. The thiouracil-treated patients received 1/10 gm. thiouracil four times daily together with 5 capsules of solubilized liver for each 0.1 gm. thiouracil. When the galactose index approached normal the dose of thiouracil was reduced to 0.1 gm. twice daily as maintenance dose. The patients being treated medically received this dosage for nine months to one year; they were then seen at regular intervals of three to six months to determine whether toxic symptoms had recurred. Those patients being prepared for thyroidectomy were treated in the same manner initially, but after a maintenance dose had been established, and both basal metabolism and galactose thyroid function tests were normal, the thiouracil was discontinued and 15 drops of Lugol's solution given three times daily, the galactose thyroid function test being employed as means of indicating when involution of the thyroid gland was complete. The patients treated with propylthiouracil received a dosage of 50 mgm. four times daily, the same plan being adopted for the maintenance dose as in the thiouracil-treated patients; when both basal metabolism and galactose thyroid function test were within normal range the dose of propylthiouracil was reduced to one-half. Ten patients were given 5 drops of Lugol's solution twice daily in conjunction with 50 mgm. propylthiouracil four times daily.

The results indicated that propylthiouracil was less toxic and more potent than thiouracil and could apparently be used with relative impunity in thiouracil-treated patients. In the thiouracil-treated group it was found that the prophylactic use of solubilized liver as a source of folic acid failed to prevent the occurrence of 1 case of agranulocytosis, 1 of granulopenia, and 2 of leucopenia, and that neither the use of pyridoxine intravenously nor large doses of folic acid stimulated granulocytosis. Ten of fifteen patients treated medically with thiouracil showed a remission of from 7 to 23 months. It is stated that "the pre-surgical preparation of thyrotoxic patients with the antithyroid drugs lessens the mortality rate and decreases the period of hospitalization".

Penicillin Therapy in Diphtheria

THE results of penicillin therapy during an outbreak of diphtheria at Gdańsk in Poland in 1946 are recorded by S. J. Wszelaki and L. J. Handzel (*Acta Medica Scandinavica*, 1948, 129, 493). Following a preliminary series of cases treated in January–May 1946, in which penicillin was

average in cases of duodenal ulcer, both in volume and acidity. I estimate 0.5 gm. of HCl in the whole of the aspirated night secretion to be very roughly the upper limit of normality. No striking difference from normal has been observed in gastric ulcer patients.

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WILLIAM MACARTHUR, K.C.B., D.S.O., M.D.,

F.R.C.P.

of a 10 per cent. solution, with minimum four doses, and maximum twenty-four doses. In most cases improvement was noted on the second day, i.e., after eight doses of 10 c.cm. calcium—the tremor, optic hallucinations, and sleeplessness disappeared. In two cases treatment had to be continued for several days before the disappearance of acute symptoms. It is stated that the use of hypnotics in delirium tremens is contraindicated.

The Oxytocic Action of Methergine

METHERGINE, a partially synthesized ergot alkaloid known as methylergonovine, has been used in the third stage of labour, immediately after the birth of the infant, to facilitate the delivery of the placenta in 711 cases, of which 269 were primiparæ and 442 multiparæ (J. E. Tritsch, E. Schneider, and E. F. Longworth: *New York State Journal of Medicine*, February 1, 1948, 48, 293). The dosage employed was 1 c.cm. of methergine, containing 0.2 mgm. per c.cm., by intravenous route. The average blood loss was 115.17 c.cm. (gross); the average length of the third stage was 7.01 minutes; incarceration of the placenta occurred in 0.86 per cent. of cases, all easily removed. In conclusion it is stated that methergine proved to be non-toxic, its use seemed definitely to reduce post-partum blood loss and accelerated the delivery of the placenta by about 3½ minutes on the average.

The Sedimentation Rate in Early Remission of Pernicious Anæmia

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provement of the sedimentation rate before the reticulocyte crisis in two cases, simultaneously in five, and in one without reticulocytosis. In the remaining ten cases liver preparations were given in conjunction with the worm remedy; an early reduction of sedimentation rate was observed when the rate had been initially raised, but this tendency was absent when the initial sedimentation rate was low. In those cases in which a combined syphilitic infection was present, no permanent improvement in the sedimentation rate and blood picture was obtained unless combined syphilitic and anti-anæmic treatment was given. On the basis of the results of the investigation it is concluded that "the sedimentation rate may serve much earlier than the erythrocyte count as a criterion of beginning remission in the majority of cases of pernicious anæmia".

The Sedimentation Rate in Abortion

IN spontaneous complete and incomplete abortion the sedimentation rate is raised. In the post-abortion period, diminution of erythrocytes in the sediment, raising of sedimentation rate, and occasionally progressively positive Takata-Ara reaction suggest the existence of complications. As a diagnostic and prognostic aid the sedimentation rate is superior to all other tests and, although not absolutely specific, is of value because of its simplicity. The time abortion occurs does not affect the sedimentation rate values. After evacuation of the uterus the figure is increased. A figure of 25 to 30 after evacuation of the uterus usually means clinical deterioration. The postoperative course will be normal if the figure is under 10 mm. The sedimentation rate tends to decrease and return to normal limits within about six days, when prognosis is favourable and recovery prompt (A. de Marchi: *Archivio di Obstetricia e Ginecologia*, November-December 1947, 52, 361). In afebrile incomplete abortion occurring in the second month there was normal recovery in 46.8 per cent.; in 53.15 per cent. the tests showed deterioration, even though the course was apparently normal, there being evidence later of genital inflammation. In abortions in the third month the percentages were similar—40 per cent. with normal recovery, 60 per cent. with persisting genital inflammation. The Takata-Ara reaction was absolutely positive in only two out of a hundred cases. These patients were subsequently found to have cholecystitis. In 20 cases the reaction was partly positive; 15 of these showed increased sedimentation rate. In some cases, however, the Takata-Ara reaction was positive when the sedimentation rate was slow, and negative when the sedimentation rate was rapid.

used with success in cases refractory to serum therapy and in those in which the use of heterogeneous albumin serum was contraindicated, a further observation was carried out between June–December 1946. The patients were divided into three groups: in the first, serum therapy was used exclusively; in the second, serum and penicillin combined; and in the third, penicillin exclusively. In the first group several cases proved refractory to serum therapy and penicillin was given in addition. In the second group there were four deaths, and in the third group, one, a child admitted in an advanced stage of the disease who died the following day. With serum therapy disappearance of fever occurred between the third and eighth day—average 4.9; with penicillin, the fever disappeared between the second and sixth day—average 3. There was disappearance of membrane with serum therapy between the third and eleventh day—average 6; with penicillin between the third and eleventh day—average 4. The dosage of penicillin employed averaged 100,000 Oxford units daily; in severe cases higher dosage was used. A comparison of the mortality figures for the last seven months of 1945 and 1946 showed that the mortality rate for the former was 25 per cent. and for 1946, only 5 per cent. It is stated that this decrease must be attributed to the improved methods of treatment, including penicillin therapy. It was found that penicillin acted more quickly and efficiently than serum alone on the growth and spread of the diphtheria organisms, and as an agent against secondary infection, such as *B. streptococcus* and the Plaut-Vincent syndrome, penicillin was the method of choice.

The Excretion of Drugs in Milk

AMONG drugs which have been found to be excreted in mothers' milk are sodium bromide, phenobarbitone, pentothal, sulphanilamide, nicotine, sodium salicylate, quinine, and aloin and phenolphthalein given as purgatives (J. H. Burn: *British Medical Bulletin*, 1947, 5, 190). Sodium bromide, which was given to ten women in dosage of 6 gm. daily for three to five days, was found in 37 out of 38 samples of milk, and in four of the infants there was clinical evidence of bromism. Phenobarbitone has been found in the milk of mothers receiving 2 grains (0.13 gm.) daily, but there was no evidence of any effect on the infants. Following administration of pentothal for excision of a branchial cyst in a woman twelve days post-partum, a barbiturate concentration of 2 mgm./100 c.cm. was present in the milk from the right breast fourteen minutes after the injection. Neither morphine nor codeine has been found in the mother's milk,

although as much as 128 mgm. morphine was given by injection in one case, and another codeine by mouth, 32 mgm. for hourly, up to a total of 192 mgm. Sodium salicylate, given in dosage of 0.6 to 4 gm. to febrile patients, was present in the milk in quantities 0.02 to 1 mgm. four hours after the last dose in each case, and also traces of quinine were present in the milk of two women to whom five doses of 300 mgm. quinine sulphate were given and in four who received 7 doses of 640 mgm. in one case thirty minutes after ingestion. Sulphanilamide has been found in the breast milk of women receiving 2 gm and 4 gm.; in a former instance in amounts of 3.8 to 13.7 mg over three days, and in the latter in amounts 11.7 to 54 mgm. Although nicotine has been found in the milk of smoking mothers, its babies were apparently unaffected even when the amount present was as high as 0.75 mg per litre. The bowels of 11 out of 33 babies were affected when aloin was given as a purgative to the mother on the fifth post-partum day, although evidence of aloin in the milk was only present in 7 of 11 cases tested. Likewise phenolphthalein affected the bowels of 10 out of 11 infants, but there was no evidence of its presence in the milk. The report concludes with a note on DDT and the possibility of the introduction of the drug into the milk of cattle partaking of foliage which has been sprayed by the insecticide. In this connexion the investigators concluded that "intensive research was necessary, the toxicity of milk from cows ingesting DDT sprayed foliage".

Calcium "Stoss" Therapy in Delirium Tremens

TWENTY-NINE cases of delirium tremens, of age ranging from twenty to fifty years, were treated with calcium (Sandoz) in high dosage, and the results are recorded by Z. Klimo (*Praxis* February 19, 1948, 37, 135). Each patient received 40 to 60 c.cm. of 10 per cent. calcium solution daily, i.e. 1 to 3 ampoules, by intravenous and intramuscular route. For the intravenous administration a 20 per cent. solution was employed. In conjunction with the calcium therapy, vitamins B₁ and C, and cardiac medications were given by mouth. The results began to appear two to three days after the beginning of treatment, when the patient slept. At the end of the acute stage, which concluded with a long sleep, 10 c.cm. of 10 per cent. calcium solution were given daily with 10 c.cm. glucose, 20 per cent. solution, and 10 to 20 units of insulin. The duration of treatment was from 3 to 6 days, average 15 days. The average total dosage of calcium employed was 10 doses of 10 c.cm.

of a 10 per cent. solution, with minimum four doses, and maximum twenty-four doses. In most cases improvement was noted on the second day, i.e., after eight doses of 10 c.cm. calcium—the tremor, optic hallucinations, and sleeplessness disappeared. In two cases treatment had to be continued for several days before the disappearance of acute symptoms. It is stated that the use of hypnotics in delirium tremens is contraindicated.

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REVIEWS OF BOOKS

Progress in Clinical Medicine. EDITED BY RAYMOND DALEY, M.D., M.R.C.P., and HENRY G. MILLER, M.D., M.R.C.P., D.P.M. London: J. & A. Churchill Ltd., 1948. Pp. xi and 356. Figures 39. Price 21s.

THE editors, assisted by ten physicians, wisely chosen for exceptional knowledge of their subjects, have produced a book dealing in a highly practical manner with the major advances in clinical medicine. All the main systems of the body of especial interest to the general physician are considered, as also venereal diseases, tropical medicine, metabolic disorders, psychomatic medicine, and the control of infections. In view of the rapid development of knowledge of the properties and value of the antibiotics, it is a matter of congratulation to find this subject discussed with such lucidity and economy of expression, without the common failing of exclusion of important information. Few criticisms can be made. In the treatment of venous thrombosis it might be wiser to recommend the maintenance of the prothrombin level at a percentage (e.g. 100) above the normal for the individual, rather than to rely on 30 to 35 seconds as the safety level. The test is so sensitive to slight differences of technique that the latter method is fraught with hazard. We are told that ankylosing spondylitis is often erroneously treated as a clinical entity separate from rheumatoid arthritis. In the next edition the author should either delete this statement, or elaborate it to justify a highly contentious remark. The sections on lung abscess and pulmonary neoplasms, although excellent in themselves, contain no strikingly new material and scarcely justify their inclusion in a book of this order. The work is well illustrated and the publishers are to be congratulated on the high standard of production.

Hearing Aids: An Experimental Study of Design Objectives. BY HALLOWELL DAVIS, S. S. STEVENS, R. H. NICHOLS, JUN., C. V. HUDGINS, R. J. MARQUIS, G. E. PETERSON and D. A. ROSS. London: Oxford University Press, 1947. Pp. viii and 197. Price 11s. 6d.

THIS study comes from the Electro-Acoustic and Psycho-Acoustic Laboratories of Harvard University, and is closely related to the work of the Committee on Electro-Acoustics of the Medical Research Council in this country, which recently published its report (*Med. Res. Coun. Rep.*, No. 261, 1947). The war gave an impetus to this work in two directions: first, the develop-

ment for military purposes of new electrical equipment, particularly miniature radio valve and telephones, which lent themselves to incorporation in hearing-aids of higher efficiency and greater convenience than those previously available; second, war-deafened veterans set the pensions hospitals the task of choosing the best from the dozens of hearing-aids on the commercial market, and so necessitated the testing and evaluation of current models. Dr. Hallowell Davis and his colleagues came to the conclusion that the differences between models of the leading manufacturers were relatively slight and future improvement will probably not be great; none of the present models brings speech to the defective ear with the crisp clarity that is needed for maximal intelligibility under conditions of noise and stress. The authors are of opinion, as a result of their investigations, that it is a fallacy that hearing-aids, like eyeglasses, must be "fitted" to the detailed idiosyncrasies of the individual impairment, and, on the contrary, that the electro-acoustic properties best suited to one type of hearing loss are those best suited to all, or nearly all. Regardless of the nature of their particular defect, most patients hear best with an instrument which amplifies all frequencies uniformly, or with moderate emphasis of the higher frequencies. A single versatile instrument of appropriate general characteristics, with a variable tone control and a semi-permanent adjustment of maximum acoustic output, is best; but even with the most perfect hearing-aid not all cases will achieve entirely satisfactory results. Proper indoctrination in the use of a hearing-aid and subsequent auditory training will continue to be of great importance for the severely hard of hearing. This is an important monograph, well and unusually produced by having the typescript of each page photographically reproduced.

Penicillin in Syphilis. BY JOSEPH EARLE MOORE, M.D. Oxford: Blackwell Scientific Publications Ltd., 1948. Pp. x and 319. Figures 57. Price 27s. 6d.

FORTY-FOUR American clinics have been coordinated for a nation-wide study of the action of penicillin in syphilis, and Dr. Moore, as chairman of the responsible subcommittees, is in a unique position to present concrete facts concerning the many thousands of patients treated. Much of the early work had to be reviewed afresh in the light of more recent knowledge concerning the varying amounts of the penicillin fractions G, F, X and K and the total dosage present in a given ampoule of com-

mercial penicillin. Data concerning early syphilis, containing the pooled experience of 25,000 treated cases, cover schedules of commercial penicillin in aqueous solution up to 2.4 mega units, and followed for eleven to eighteen months. Special attention is paid to the rationale and technique of penicillin in oil-beeswax preparations, and these sections especially should be studied by all practitioners. A chapter is also devoted to the masking of incubating syphilis by penicillin given for gonorrhœa, and the importance of watching these cases for at least four months after treatment is stressed. Other chapters include the pharmacology of penicillin, penicillin in experimental syphilis, and the effects of the drug on latent, cardiovascular, ocular, congenital, prenatal and neuro-syphilis. The book, which is identical with that published in the U.S.A., has a large number of interesting graphs and tables and an extensive bibliography which, by reason of last minute additions, is complete to October 1946. This important work is of the excellence expected of the author of "The Modern Treatment of Syphilis" and should be read by all who are ever called upon to give a dose of penicillin for venereal disease.

The Child's Lung: Developmental Anatomy, Physiology and Pathology. BY STEFAN ENGEL, M.D. London: Edward Arnold & Co., 1947. Pp. viii and 332. Illustrations 283. Price 40s.

THE primary object of this monograph is to emphasize the importance of the anatomical approach to pulmonary physiology and pathology in childhood. The author has given a detailed presentation of the anatomical features of the thorax, bronchial tree and lungs in each age-group: this is fundamentally important, since the anatomical features change so much in the growing child. Physiological characteristics and pathological peculiarities are correlated with the anatomical features in each age-group. The book is well produced and liberally illustrated with diagrams and photomicrographs.

The Secret Instrument. BY WALTER RADCLIFFE. London: Wm. Heinemann (Medical Books) Ltd., 1947. Pp. xvi and 83. Figures 23. Price 10s. 6d.

DR. RADCLIFFE provides a well-written and interesting account of the invention of the obstetric forceps by the Chamberlen family in the 16th century and the evolution of the modern instrument. The history of the Chamberlens and the attempts of others to discover the secret of the forceps which the family held for over a hundred years makes enjoyable reading.

NEW EDITIONS

THE fifth edition of *Medicine: Essentials for Practitioners and Students*, by G. E. Beaumont, D.M., F.R.C.P., D.P.H. (J. & A. Churchill Ltd., 30s.), contains a number of new articles dealing respectively with infective hepatitis, erythroblastosis, scrub typhus, fibrocystic disease of the pancreas, primary atypical pneumonia, congenital agenesis of the lung, œstrogens in the treatment of carcinoma of the prostate, thiouracil in thyrotoxicosis, homologous serum jaundice, aspirin and phenol poisoning.

Modern Drugs in General Practice, by Ethel Browning, M.D., CH.B., in its second edition (Edward Arnold & Co., 12s. 6d.) contains a chapter on penicillin with methods of administration and clinical indications. Developments in the use of the sulphonamide drugs, and a number of new antiseptics are also among the new material.

MUCH new material has been added to *The American Illustrated Medical Dictionary*, by W. A. Newman Dorland, A.M., M.D., F.A.C.S., in its twenty-first edition (W. B. Saunders Co., Ltd., 40s.), representing the many advances in medicine, surgery, biochemistry and pharmacology during the war years. A useful table of preparations with dosage in both apothecaries and metric systems is included.

Year Book of General Medicine, 1947, edited by George F. Dick, M.D., and colleagues (Year Book Publishers Inc., Chicago: H. K. Lewis & Co., 21s.), contains among a wealth of new material sections on the control of air-borne infection by the use of triethylene glycol vapour, BCG inoculation in the prophylaxis of tuberculosis, the use of the antihistamine drugs in asthma, folic acid in the treatment of macrocytic anæmia, and the prophylactic use of formalized mumps virus.

NEW sections on typhus, glandular and undulant fevers, influenza, and encephalitis lethargica have been added to *Essentials of Fevers*, by Gerald E. Breen, M.D., B.Ch., D.P.H., D.O.M.S., in its second edition (E. & S. Livingstone Ltd., 15s.), and much new material has been included in other sections. The appearance of the new edition of this book on fevers, which has been out of print for some time, is welcome.

HALE-WHITE'S *Materia Medica, Pharmacy, Pharmacology and Therapeutics*, revised by A. H. Douthwaite, M.D., F.R.C.P., in its twenty-seventh edition (J. & A. Churchill Ltd., 15s.) has been subjected to complete revision. Sections on the antibiotics, curare, benadryl, and DDT are among the many additions, and the sections on sex hormones have been revised.

NOTES AND PREPARATIONS

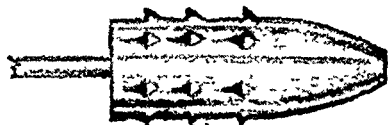
NEW PREPARATIONS

DEPROPANEX (deproteinated pancreatic extract) is an antispasmodic substance which is stated to have been used with success in the treatment of intermittent claudication associated with arterial disease, peripheral vascular disease, renal and ureteral colic, and dysmenorrhœa. It is supplied in rubber-capped vials of 10 c.cm. for intramuscular injection, price 21s. plus 4s. 8d. purchase tax, by Sharp and Dohme Ltd., West Hill Laboratories, Hoddesdon, Herts.

IMMUNE SERUM GLOBULIN (HUMAN): LEDERLE
—Prepared from human placentas for use in the treatment and prophylaxis of measles, this new concentrated human serum globulin is stated to contain approximately 16 per cent. gamma globulin. It is claimed that timely administration not only prevents or modifies the attack but also lessens the incidence of complications. The manufacturers are Lederle Laboratories Division: Distributors—Cyanamid Products Ltd., Brettenham House, Lancaster Place, London, W.C.2.

A NEW VARICOSE VEIN NEEDLE

A new varicose vein needle with a roughened head, which scarifies the venous intima and so produces a more perfect thrombosis than when a sclerosant only is employed, has recently been placed on the market. Other advantages claimed for the needle, of which an enlarged view of the head is shown in the illustration, are that the



rocket-shaped nose facilitates entry into the vein, and gentle manipulation of the pliant shaft will traumatize the intima without unnecessary damage. The manufacturers are John Bell & Croyden, Wigmore Street, London, W.1, who have produced the needle for Mr. Rowden Foote.

HUNGARIAN CENTENARY CONGRESS OF PÆDIATRICS

THE Hungarian Medical Trade Union is arranging a medical convention in Budapest between September 4-12, 1948, during which period the Pædiatric Section will organize an International Congress of Pædiatrics. Two of the five days will be devoted to plenary sessions of all sections, and on three days "Rheumatic Fever", "Toxicosis" and the "Social Signifi-

cance and Results of Pædiatrics" will be the topics for discussion. All pædiatricians are invited to participate. Full particulars can be obtained from the Centenary Congress Committee, Bokay Janos u.53, Budapest 8, Hungary.

MEDICAL FILMS

At the Southern Counties Medical Exhibition to be held at the Polygon Hotel, Southampton April 20-22, a programme of medical films will be presented each day at 3 p.m. Among the films to be shown are several dealing with the subject of anaesthesia.

Curare film.—A film on *d*-tubocurarin chloride, prepared by the Wellcome Film Unit was shown at the Wellcome Research Institute on February 19. The film, which is in colour, demonstrates the effect of the drug when used experimentally and in surgical practice. It is now available for exhibition to practitioners and students. Applications should be made to the Wellcome Film Unit, the Wellcome Research Institution, 183-193 Euston Road London, N.W.1.

NAPT MEDICO-SOCIAL SECTION

THE Inaugural Meeting of the NAPT Medico Social Section will be held on Friday, May 7 1948, at 5 p.m. at the British Medical Association House, Tavistock Square, London, W.C.1. Sir Robert Arthur Young, C.B.E., Vice-Chairman of the Council of the NAPT, will preside and Mr. Anthony Greenwood, M.P., will address the meeting on "Social Aspects of Tuberculosis".

THE EMERGENCY BED SERVICE

THE Emergency Bed Service (E.B.S.) of King Edward's Hospital Fund for London, which for nearly ten years has assisted general practitioners in finding hospital beds for acute cases, has decided to extend its functions to provide information on other points connected with their work, such as the time and place of out-patient clinics, ambulance services, and agencies for the help of chronic patients. Inquiries should be addressed to MONarch 3000. The address of the E.B.S. is 10 Old Jewry, London, E.C.2.

Change of address: Owing to the termination of their lease F.H. Lilly and Company Ltd. have vacated the offices at 2-4 Dean Street, London, W.1, and all future correspondence should be addressed to them at Basingstoke.

The contents of the May issue, which will include a symposium on "Diseases of the Skin", will be found on page 1xxiv at the end of the advertisement section.



ATOPIC AND ALLERGIC DISTURBANCES OF THE SKIN

By R. M. B. MACKENNA, M.D., F.R.C.P.

*Physician in Charge of the Dermatological Department, St. Bartholomew's
Hospital; Physician, St. John's Hospital for Diseases of the Skin.*

FOR present purposes I shall adopt a well-known definition and say that "allergy is a state of altered reactivity of the skin as a result of previous contact with an allergen or antigen". This alteration in reactivity is caused by the first exposure to the allergen or antigen, but is made manifest by subsequent contacts. To a much greater degree than is usually realized the phenomenon is a principal factor in the etiology of many eruptions, and modifies the course of many more; for example, some of the eruptions of secondary syphilis have been regarded as allergic, and there are numerous rashes which may be referred to as "toxic erythema" which are visible manifestations of allergic phenomena.

Atopy is a subject which has not received much attention in general medical literature in this country. The atopic individual has an inborn tendency to react and but little tendency to exhibit fixed allergic patterns; he is a stage beyond the allergic person. J. H. Stokes (1942) has emphasized that in differentiating atopic from allergic subjects the significant factor is the inveterate propensity of the former to react, a propensity which extends to every part of their being and leads to non-striated muscle crises, disturbed mental reactions, paroxysms of itching, and inflammatory responses of their skins. The person suffering from the eczema-asthma-hay fever syndrome is the typical example of the atopic individual.

ATOPIC DERMATITIS

The name "atopy" is said to be derived from the Greek *ἀτομία*, which means "strangeness" or "oddness", and thus by implication has been translated as "a strange disease". The term was first used by Coca (1926) to define certain clinical forms of human hypersensitiveness that do not occur, so far as is known, in the lower animals, and which are subject to hereditary influence. The substances to which atopic patients are sensitive are called *atopens*, and the antibody-like substances found in their blood sera are called *reagins*. The latter are said to differ from anaphylactic antibodies. It has been suggested that atopens may be absorbed through the skin and other "surface membranes".

An atopic eruption may be diagnosed if the following postulates are fulfilled:—(1) There is a family history of asthma, hay fever or eczema; (2) a personal history which reveals other atopic manifestations; (3) the demonstration of passive transfer of sensitization. When dealing with infants it is often impossible for all these postulates to be fulfilled, but as an accurate family history can usually be obtained, and as eczema is the presenting symptom in 90 per cent. of atopic cases, "atopic eczema" can be diagnosed in babies with some accuracy.

Sensitivity test.—The mechanism of passive transfer of sensitivity was first demonstrated by Prausnitz and Küstner (1921) and is now often called the P-K reaction.

To make this test in the most simple way a small amount of the blood serum (0.05 c.cm.) from a sensitive person is injected into the skin of an insensitive individual. In atopic states, reagins are present in the blood, and injections of reagin-containing serum transfer the specific sensitivity to the injected site. Therefore when, a few days later, a small amount of the sensitizing agent is injected into the same site, a reaction occurs which as a rule is indicated by the formation of a wheal. Needless to say suitable controls are used.

It should be noted that not all cases of infantile eczema are "atopic", for the hereditary factor, which is essential in atopy, may be absent. Stokes and his colleagues (1942) believe that the eczemas of childhood are more often allergic than atopic.

Clinical signs.—The atopic child may not be as fat and well nourished as the child with allergic eczema; often the eruption begins on the face and then extends to the body and limbs, where the flexural aspects are more severely affected than the extensor. Itching and restlessness are marked features, but despite all their discomfort the children thrive fairly well, and often, as in pink disease, the mothers look more exhausted and seem more disturbed than their offspring. All phases of the eczema reaction (erythema, papule and vesicle formation, oozing and scaling) may be seen, and the eruption may be complicated by secondary infection.

Most cases of infantile eczema improve about the age of two years, but in some—the true atopic individuals—a leathery lichenification of the skin develops on the flexor surfaces of the elbows, wrists and knees. The neck may be affected. From time to time, for no apparent cause, the lesions itch excessively and change their nature and ooze, whilst eczematous lesions may break out on the face and other areas. In this country the eruption thus described is usually called Besnier's prurigo. Asthma often develops and hay fever may be troublesome; the patient's life becomes the weary burden of the eczema-asthma-hay fever subject, who, nevertheless, seldom refrains from procreation when he becomes adult and thus inflicts on succeeding generations the affliction of his life.

Stokes (1942) has stated that "the allergic skin, like the average nervous system, may go through prostration once or even twice, and recover on removal of an excitant and the correction of one or two predisposing causes.

The skin of the atopic individual is in such a state of constant protesting hyper-irritability, that no sooner is it relieved of one set of contacts and excitants than it seizes upon another group and explodes or prostrates with renewed vigour”.

CONTACT DERMATITIS

The substances which cause contact dermatitis are of two groups: primary irritants and cutaneous sensitizers. The former will cause inflammation of human skin by direct chemical or physical action, provided they are in sufficient concentration and the exposure to their action is sufficiently prolonged. Strong inorganic acids and alkalis are primary irritants; so in a broader sense, are X-rays, the beta rays of radium, and ultra-violet rays. These do not come within the scope of this article.

The cutaneous sensitizers do not affect normal skin immediately, and, in general, the majority of persons exposed to their action do not become sensitized. Their action is insidious, and relatively long-continued exposure to them is necessary before the resistance of the skin diminishes and dermatitis is produced. The range of cutaneous sensitizers is enormous and space does not allow any attempt at a brief classification here. They extend from the juices of lily bulbs (which cause much trouble to horticulturalists in certain areas) to the paraphenylenediamine used by the tipper of furs; from the “improvers” put into flour to the lacquer applied to finger nails; from the cement mixed by a navvy to the alkaline powder used by a housewife to clean the bath.

In most cases of contact dermatitis of this type there must be a personal factor, although most dermatologists are reluctant to commit themselves in this matter. Many persons can handle sensitizers for many years without ill effect; a few become sensitized. It is not therefore irrational to suggest that sensitization develops as a result of some fault in the biochemistry of the skin, and postulate (knowing well the arguments against such a theory) that if a cement worker who develops occupational dermatitis at the age of forty-nine had entered another trade as a youth, and had been exposed to a different sensitizer of similar potency for the same period, he would very probably have developed signs of sensitization to that other substance at about the same age.

There is a widely held clinical impression—not statistically confirmed—that the number of cases of contact dermatitis is increasing; this is due in part to the increasing use, both in domestic and industrial life, of sensitizing agents, including detergents, wetting agents, and emulsifiers, in part to the greater numbers of the population at risk now that there is little unemployment, and—in the domestic sphere—that most housewives have to do their own housework. The prolonged limitation of proteins and fats in the national diet may also be a factor which should be considered.

It is convenient to subdivide the group of dermatitis here considered into

two sections: eruptions which occur because of occupational contacts, and those which occur from other risks. It should be remembered that few industries are free from risk, and that the prevention of occupational dermatitis is much more important than the relief of its symptoms.

Preventive measures.—Sybil Horner (1942) has emphasized that four factors are of major importance: these are, selection, protection, inspection, and cleanliness. The selection of personnel who are to be exposed to industrial hazards so that, for example, men with dry or ichthyotic skins are excluded from contact with degreasing agents, or men with moist, sweaty skins from dusts which are activated by moisture, and so on. The protection of workers from deleterious liquids (by adequate shielding of machinery), from noxious dusts or vapours (by adequate ventilation), from constant contact with hazardous agents (by the use of carefully selected barrier creams or suitable clothing) is also of importance. Inspection is always necessary, for human beings, both employers and employees, are fallible, and frequent exposure to a danger breeds a certain contempt from which springs negligence in maintaining the protective routines which have been devised. Finally, cleanliness: the simple removal, without injury, of deleterious agents from the skin during the midday break and also on leaving work in the afternoon, is of great value.

Non-industrial contacts.—Dermatitis may result from sensitization to fabrics, or to dyes or other chemicals with which the fabrics have been treated; from the rubber of gloves, corsets or brassières, the nickel or chromium plating of wrist watches or suspenders, the plastic material of spectacle frames, and from many other causes. It is well to remember that dermatitis of the eyelids may be due to sensitivity to nail-lacquer, even though the skin of the fingers is not inflamed. In housework, cleaning agents varying from washing soda to organic detergents, bleaching agents, metal or furniture polish, or even insecticides, may be inculpatated.

Organic chemistry has hitherto been concerned only with compounds of carbon; if it is true, as I am informed, that a complete organic series of each of several other elements is now within the range of chemical achievement, it will be interesting to see if the exploitation of this fact increases or diminishes the dermatological problems by which we are beset. Nevertheless, nature is still fairly prolific in producing sensitizers, and every year we see fresh cases of dermatitis due to sensitization to common flowers such as primulae or chrysanthemums.

Diagnosis.—In general it may be said that most contact dermatitis begin with erythema and pass through a stage of papule and vesicle formation. The vesicles burst, or are opened by rubbing and scratching, and then dry, so that the skin becomes scaly and then heals. The eruption may be complicated by pyogenic infection. In diagnosis, history taking is of vital importance. It is necessary to know where the eruption began, because it is reasonable to assume that contact dermatitis will originate on the most

vulnerable areas of the sites most exposed to the sensitizing agent. In this connexion dusts are more "tricky" than liquid sensitizers, for a man who handles an irritant dust may always wash his hands immediately after exposure to it, but be unaware that the dust blows upwards so that some of it lodges under his collar and remains there for several hours, eventually causing the dermatitis first to occur on his neck.

The path of extension of the rash is the next matter to consider. Many occupational dermatites start on the fingers and webs, spread thence to the backs of the hands and then to the forearms. Other areas are not involved. If, for example, a man states that he first noted a rash on his forearms and says that the areas next involved were the front of the chest and the groins, there is considerable probability (i) that the eruption did not first develop on the forearms but was only first noticed there, and (ii) that he has *seborrhœic dermatitis* with signs of the eruption also to be found on such areas of his body as the interscapular area and behind his ears.

Other matters which demand inquiry are the previous dermatological history of the patient, for he may, for example, be an *ichthyotic* or a *psoriatic*, and this knowledge may assist diagnosis. The previous general medical history and the treatment which has been applied before the patient seeks assistance are both of importance; he may perhaps know that he suffers from *leukæmia* and the eruption may be a *leukæmic infiltration*, whilst previous treatment may have produced *dermatitis medicamentosa*, or so modified the appearance of the eruption as to make diagnosis difficult. There are other questions, but the exigencies of space prevent their inclusion. With some temerity I should like to mention that whilst few practitioners bother to test the urine in these cases no dermatologist can afford not to do so. Further, in the study of any allergic condition an assessment of the psychological background is well worth making.

The detection of the sensitizer in many cases which originate in the home often demands the ability of a Sherlock Holmes. Often patients are sceptical and therefore uncooperative when they are told that their symptoms are due to exposure to some frequently encountered but nevertheless simple hazard. Much tact and persuasion may be necessary before the problem is solved. With an intelligent person it may be worth suggesting that he should keep a diary and write down in it a brief note of everything he does each day, and a note as to the state of his skin. By a study of the diary it is sometimes possible to obtain a clue which will lead to the solution of the problem.

Patch testing with suspected sensitizers often gives conflicting results, but if it is to be undertaken the practitioner would do well to consult the articles on the subject by Sulzberger and Baer (1943, 1944).

DRUG ERUPTIONS

Of these little will be said, except to emphasize that when an eruption develops from the ingestion of a drug, four matters have to be considered:—

(1) The patient may be sensitized to the drug, in which case the eruption develops shortly after the first few doses are taken. (2) The eruption may be due to the toxic effect produced by simple or cumulative overdosage. (3) The rash may develop when overdosage has been avoided but when the patient has continued to take the drug for a period and has become sensitized. This period varies considerably with the nature of the drug. With sulphonamides a period of ingestion of longer than eight days may lead to a sulphonamide eruption. (4) In certain maladies the liberation of toxins from organisms destroyed by the drug may lead either to an exacerbation of the original cutaneous symptoms or to the appearance of a new eruption.

The phenomenon of "fixed eruption" is not widely known. In relatively few persons, certain drugs, particularly phenolphthalein, phenacetin and acetanilid, but also barbiturates and salicylates, cause the appearance on a localized area of erythema, erythematous papules or wheals, which arise after taking the drug and recur on the same site whenever the same drug is taken again. Usually these areas itch, and a chronic lichenification may develop on them; this persists because the patient keeps rubbing the skin. Dermatitis medicamentosa must be mentioned only to be dismissed with the observation that despite the reiterated warnings of dermatologists (Barber, 1944) sulphonamide dermatitis is still prevalent, acriflavine dermatitis is not uncommon, and dermatitis from penicillin, or from the vehicle in which the penicillin is incorporated for local application, is of frequent occurrence.

URTICARIA

Little need be said about urticaria caused by food. The attack may be acute and transitory, as when a patient who knows he cannot eat shell fish without paying the penalty takes oysters at a banquet, or it may be chronic and of obscure origin. I can recall a patient who was sensitized to Angostura bitters, and another who was sensitized to some ingredient in English bread (she could eat bread in France with impunity); these types of urticaria of unusual etiology require much careful investigation before the cause can be detected. Some urticarias are psychogenic in origin and perpetuation. When dealing with a case of obscure origin it should be remembered that a septic focus is an occasional cause of the eruption and the necessary search for such a cause should not be omitted. In a number of cases the cause is not discovered and treatment must be symptomatic.

The so-called *papular urticaria*, lichen urticatus, or heat spots from which children suffer is an interesting condition. Whilst in many cases it appears to be provoked by eating certain foods, small berried fruits such as gooseberries often being suspected, Hallam (1932) showed that the home environment was often associated with the cause. Certainly the majority of these eruptions disappear without treatment if the children are taken into hospital, and in practice it is often sensible to advise that the child should change his environment by, for example, being sent to stay with a relation.

Unfortunately this is only a palliative remedy, for the eruption may recur when the child returns home. The correct approach would seem to be a psychological one, but as this involves the parents as well as the patient it is not often practicable.

TREATMENT

This is such a vast subject that only a few aspects will be considered. Obviously, when dealing with an eruption believed to be allergic, the first thing to be done is to discover the agent to which the patient is sensitized and ensure that he is not again exposed to it. Unfortunately many have polyvalent sensitivities and it is difficult to discover them all. Also in many types of allergic reaction there are other factors, particularly psychological ones, which thwart the physician's best endeavours.

Desensitization may be attempted by means of specific or non-specific methods. The former can be most dangerous if not carried out by an expert; the latter often fail. Such measures as peptone injections and autohæmotherapy are so well known that they do not require any comment. The introduction of lertigon (a synthetic histamine-protein complex: Parke Davis & Co.) has been helpful. This is administered by subcutaneous injection in increasing doses at intervals of four to five days.

Antihistamine drugs.—The introduction of antihistamine agents is one of the greatest advances in recent years. Ungar, Parrot and Bovet (1937), following up the work of Fournau and Bovet (1933), demonstrated that certain phenolic esters possessed the property of counteracting the action of histamine. Since then a number of these esters have been synthesized, including benadryl, pyribenzamine, neoantergan, and antistin. Of these, benadryl, anthisan (a maleate of neoantergan) and antistin are now available in this country. It is too early to predict the ultimate place of these drugs in the therapy of allergic disorders. At present it would appear that they are all capable of controlling and modifying the symptoms of urticaria, affording relief in some 70 per cent. of the cases. Their action is somewhat variable in contact dermatitis and other cutaneous manifestations of allergy, but it is usually worth while trying whether or not they have a beneficial effect. If they are going to give relief their effect will be noted within two or three days, and it is little use continuing their administration if benefit has not accrued within this period. On benadryl, in doses of 150 mgm. daily, most adults feel sleepy for the first five days; thereafter this symptom usually passes. Because of this side-effect other sedatives are best omitted, at least until it is seen how the patient tolerates the drug. Patients often complain of drowsiness with other antihistamine agents; defects of vision, nausea, faintness, giddiness and headache are other side-effects which may be reported. The usual adult dose of benadryl is one 50-mgm. capsule, thrice daily; of anthisan and antistin, 100 mgm., three to six times daily. For children, the elixir of benadryl containing 10 mgm. of the drug in each fluid drachm is useful. It should be noted that whilst these drugs do not have a

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URTICARIA: DETECTION OF INGESTED ALLERGENS

THE SINGLE FOOD ADDITIVE DIET

BY BERNARD H. WINSTON, M.D.
AND RICHARD L. SUTTON, JUN., M.D.
Kansas City, Missouri, U.S.A.

A METHOD is presented for detecting ingested allergens productive of urticaria, a method which is effective and which lends itself to use by the general practitioner as well as by the specialist. There is need for such a method because there is general agreement that skin tests with food extracts are unreliable (Sulzberger and Rostenberg, 1935; Stokes, *et al.*, 1935; Hopkins and Kesten, 1934; Waldbott and Ascher, 1938; Urbach and Gottlieb, 1946; Rinkel, 1944). Urticaria may be of short duration or may persist for months or years despite considerable medical effort. The method herein described is designed primarily for chronic cases.

Urticaria may be due to ingested food (Rinkel, 1944), inhalant allergens (Sulzberger and Rostenberg, 1935; Rappaport and Hoffman, 1941), injected or ingested medication (Sulzberger and Rostenberg, 1935), scabies (Goldman, 1944) or other parasites, external chemical allergens, physical agents (Duke, 1925), focal infection (Sulzberger and Rostenberg, 1935), or psychosomatic disorder (Stokes, *et al.*, 1935; Menninger and Kemp, 1935). Each of these possible causes must be given consideration. In all cases the patient must be examined and the possibility of parasitic infection eliminated, internal medication capable of causing urticaria must be discontinued, and suspected external allergens eliminated. The presence of focal infection should be noted for possible subsequent eradication, and also the presence or absence of emotional instability. In some cases the influence of inhalant allergens must be determined and removed or adequately treated (Rinkel, 1944). Detection of ingested allergens must be achieved.

THE SINGLE FOOD ADDITIVE DIET

This method of detecting ingested allergens results in their identification with accuracy and does not result in nutritional deficiency. The method consists of stopping all ingested substances, then soon introducing single substances in a controlled and systematic manner so that ingesta may be identified individually as harmless or harmful. The procedure may be named the "Single Food Additive Diet". It is the antithesis of the multiple choice elimination diets such as those devised by Rowe (1934) and others, for it is a procedure of adding known items to zero rather than subtracting items from a multiplicity of things.

cumulative effect, they are only repressive in their action. If given in a case of chronic urticaria, the patient may be symptom-free while taking the drug, but the symptoms may recur as soon as it is stopped. Fortunately in many cases other measures, or the processes of nature, may have removed the cause of the malady, so that when after a period of some weeks, the antihistamine preparation is stopped, the patient may be found to be cured.

Of *general treatment* of allergic conditions, little need be said except to emphasize that much aggravation of these eruptions occurs because, at the outset, most of us have a tendency to withhold sedative drugs needlessly. In chronic allergic states it is often wise not to prescribe sedatives, but in the early stages, if sufficient sedative is administered to ensure that the patient sleeps properly and does not spend the night in a drowsy state scratching himself unmercifully, the course of his attack may be greatly curtailed.

Of *local treatment*, nursing is one of the most important features; when dealing with infants and young children it is of paramount importance. In general, the golden rule applies; briefly this implies that in acute stages lotions (calamine, 1 per cent. aqueous solution of aluminium acetate or silver nitrate), in subacute states creams or pastes (zinc cream of the B.P.C. formula, or zinc paste), in chronic states pastes or ointments, should be used. Tar, which should not be used in acute stages, is often beneficial in more indolent rashes, particularly when the skin is thickened or lichenified. It is well to begin tar therapy with a weak preparation such as solution of coal tar, 3 per cent. in zinc cream or paste, and if this is well tolerated increase the amount to 6 per cent.; but many indolent eruptions respond best to a strong tar paste containing prepared coal tar 6 to 12 per cent., zinc oxide 18 per cent., starch 36 per cent., in a base of soft paraffin. More elegant preparations such as Martindale's ether-soluble tar paste (which contains 1.5 per cent. of a soluble fraction of tar), or the colourless tar dermatological cream made by Genatosan, have their uses.

Finally, it should not be forgotten that many of the chronic eczematous types of allergic dermatoses respond best to a course of X-ray therapy, although unfortunately this is a remedy which is not always available and which cannot be used indiscriminately.

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This method of detecting ingested allergens results in their identification with accuracy and does not result in nutritional deficiency. The method consists of stopping all ingested substances, then soon introducing single substances in a controlled and systematic manner so that ingesta may be identified individually as harmless or harmful. The procedure may be named the "Single Food Additive Diet". It is the antithesis of the multiple choice elimination diets such as those devised by Rowe (1934) and others, for it is a procedure of adding known items to zero rather than subtracting items from a multiplicity of things.

Principles.—The single food additive diet is constructed upon the following principles:—

(a) In chronic urticaria, hypersensitivity is commonly due to foods that the individual likes and often eats.

(b) Dietary management is started with a vegetable and a cereal not usually eaten daily.

(c) Not more than one single food (or food component) is added per meal.

(d) A food containing more than one constituent, such as frankfurter or vegetable soup, is never added until after many individual foods have been tested.

(e) Water, non-iodized salt, and cane sugar are so rarely allergenic that they are not ordinarily tested individually, although they may be so tested. It is usually found that if rice, beef steak, and boiled ham are tolerated, then puffed rice, roast beef, veal, and bacon will be tolerated.

(f) Inasmuch as nearly all individuals with urticaria obtain relief of symptoms within four to twelve hours under this method of treatment, it has been found feasible to add a single new food at each meal so as to provide within a few days a diet possessing satisfactory variety. It is justifiable to prescribe this rapid programme for the majority of patients and to lengthen the intervals between additions of foods only in the occasional case in which longer intervals prove necessary.

Application.—The single food additive diet is applicable to all patients whose urticaria may be due to ingested allergens, and who fall into one of the following groups:—

(1) Those in whom ingested allergens are not clearly evident from the history, the anamnestic approach being a method on which little reliance may be placed.

(2) Those in whom ingested allergens may involve several foods and who cannot be relieved by elimination of only some of these; in such patients multiple-choice elimination diets, food diary, and skin tests (Sulzberger and Rostenberg, 1935; Rinkel, 1944; Rowe, 1934, 1941) would not be effective.

(3) Those in whom cyclic food allergy is present. Cyclic food allergy (Rinkel, 1944) is of three clinical types: (a) the perennial type which is a primary food allergy; (b) the concomitant type which is a food allergy that becomes manifest only when an allergen, for instance, ragweed, is also inhaled, and (c) the thermal type which is not evident until the individual is exposed to cold air or is chilled to, or below, his critical level.

PROCEDURE

In applying the single food additive diet to the patient the following things are done:—

(1) A dietary outline is given the patient, who, we shall assume, is seen in the afternoon, so that he starts with the evening meal.

(2) At each subsequent interview a list of foods already tested is given to the patient, designating those foods which have been tolerated and those apparently not tolerated.

(3) If urticaria develops following any meal, the new food added at that meal is suspected of being an allergen and is not repeated for from five to seven days. If urticaria develops upon re-testing, the food is considered to be a proved causative allergen.

(4) If one of the foods suspected is wheat, corn, eggs, or milk, a list of

foods containing the substance is given to the patient, and all such foods are prohibited until after the seven days' dietary outline is completed, following which the suspected food is re-tested.

(5) All internal medication, including vitamins, is discontinued. If medication is necessary, the medicine is tested as a new ingested substance to be tried individually.

(6) Candy, soft drinks, and liquor are prohibited until they are tested individually.

(7) A saline laxative is prescribed immediately before the start of the prescribed diet.

(8) Pyribenzamine hydrochloride, one 50-mgm. tablet, is given to the patient after the use of the saline laxative and before ingestion of the first meal if urticaria is present at that time.

DIET PROGRAMME

First day:

Office visit during afternoon. Programme initiated.

Evening meal: boiled rice (first food item tested).

Second day:

Breakfast: oatmeal (second) cooked with water.

Lunch: rice if tolerated, broiled beef (third).

Office visit during afternoon.

Evening meal: broiled beef if tolerated, boiled rice, beets (fourth).

Third day:

Breakfast: oatmeal and milk (fifth).

Lunch: milk if tolerated, beets if tolerated, boiled rice, plain gelatin (sixth).

Office visit during afternoon.

Evening meal: plain gelatin if tolerated, broiled beef, rice, beets, white bread (seventh).

Fourth day:

Breakfast: white bread if tolerated, puffed rice if rice is tolerated, milk, banana (eighth).

Lunch: boiled rice and milk, white bread, beets, plain gelatin, boiled ham (ninth).

Office visit during afternoon.

Evening meal: roast beef if beef steak is tolerated, beets, white bread, plain gelatin, peas (tenth).

Fifth day:

Breakfast: banana if tolerated, oatmeal and milk, white bread, butter (eleventh).

Lunch: butter if tolerated, boiled ham if tolerated, white bread, beets, plain gelatin, yellow corn (twelfth).

Office visit during afternoon.

Evening meal: veal chops if beef is tolerated, peas if tolerated, butter, white bread, boiled rice and milk, beets, plain gelatin, tea (thirteenth).

Sixth day:

Breakfast: tea if tolerated, puffed rice, milk, white bread, butter, banana, egg yolk (fourteenth).

Lunch: roast beef, butter, white bread, plain gelatin, beets, tea, boiled or baked white potato (fifteenth).

Office visit during afternoon.

Evening meal: yellow corn if tolerated, white bread, butter, broiled beef steak, tea, boiled rice, milk, peas, plain gelatin, pears (sixteenth).

Seventh day:

Breakfast: bacon if boiled ham is tolerated, white bread, butter, tea, milk, banana, shredded wheat (seventeenth).

Lunch: boiled or baked white potato if tolerated, white bread, butter, tea, corn, peas, beets, plain gelatin, boiled ham, Swiss cheese (eighteenth).

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(e) Water, non-iodized salt, and cane sugar are so rarely allergenic that they are not ordinarily tested individually, although they may be so tested. It is usually found that if rice, beef steak, and boiled ham are tolerated, then puffed rice, roast beef, veal, and bacon will be tolerated.

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(1) A dietary outline is given the patient, who, we shall assume, is seen in the afternoon, so that he starts with the evening meal.

(2) At each subsequent interview a list of foods already tested is given to the patient, designating those foods which have been tolerated and those apparently not tolerated.

(3) If urticaria develops following any meal, the new food added at that meal is suspected of being an allergen and is not repeated for from five to seven days. If urticaria develops upon re-testing, the food is considered to be a proved causative allergen.

(4) If one of the foods suspected is wheat, corn, eggs, or milk, a list of

foods containing the substance is given to the patient, and all such foods are prohibited until after the seven days' dietary outline is completed, following which the suspected food is re-tested.

(5) All internal medication, including vitamins, is discontinued. If medication is necessary, the medicine is tested as a new ingested substance to be tried individually.

(6) Candy, soft drinks, and liquor are prohibited until they are tested individually.

(7) A saline laxative is prescribed immediately before the start of the prescribed diet.

(8) Pyribenzamine hydrochloride, one 50-mgm. tablet, is given to the patient after the use of the saline laxative and before ingestion of the first meal if urticaria is present at that time.

DIET PROGRAMME

First day:

Office visit during afternoon. Programme initiated.

Evening meal: boiled rice (first food item tested).

Second day:

Breakfast: oatmeal (second) cooked with water.

Lunch: rice if tolerated, broiled beef (third).

Office visit during afternoon.

Evening meal: broiled beef if tolerated, boiled rice, beets (fourth).

Third day:

Breakfast: oatmeal and milk (fifth).

Lunch: milk if tolerated, beets if tolerated, boiled rice, plain gelatin (sixth).

Office visit during afternoon.

Evening meal: plain gelatin if tolerated, broiled beef, rice, beets, white bread (seventh).

Fourth day:

Breakfast: white bread if tolerated, puffed rice if rice is tolerated, milk, banana (eighth).

Lunch: boiled rice and milk, white bread, beets, plain gelatin, boiled ham (ninth).

Office visit during afternoon.

Evening meal: roast beef if beef steak is tolerated, beets, white bread, plain gelatin, peas (tenth).

Fifth day:

Breakfast: banana if tolerated, oatmeal and milk, white bread, butter (eleventh).

Lunch: butter if tolerated, boiled ham if tolerated, white bread, beets, plain gelatin, yellow corn (twelfth).

Office visit during afternoon.

Evening meal: veal chops if beef is tolerated, peas if tolerated, butter, white bread, boiled rice and milk, beets, plain gelatin, tea (thirteenth).

Sixth day:

Breakfast: tea if tolerated, puffed rice, milk, white bread, butter, banana, egg yolk (fourteenth).

Lunch: roast beef, butter, white bread, plain gelatin, beets, tea, boiled or baked white potato (fifteenth).

Office visit during afternoon.

Evening meal: yellow corn if tolerated, white bread, butter, broiled beef steak, tea, boiled rice, milk, peas, plain gelatin, pears (sixteenth).

Seventh day:

Breakfast: bacon if boiled ham is tolerated, white bread, butter, tea, milk, banana, shredded wheat (seventeenth).

Lunch: boiled or baked white potato if tolerated, white bread, butter, tea, corn, peas, beets, plain gelatin, boiled ham, Swiss cheese (eighteenth).

Principles.—The single food additive diet is constructed upon the following principles:—

(a) In chronic urticaria, hypersensitivity is commonly due to foods that the individual likes and often eats.

(b) Dietary management is started with a vegetable and a cereal not usually eaten daily.

(c) Not more than one single food (or food component) is added per meal.

(d) A food containing more than one constituent, such as frankfurter or vegetable soup, is never added until after many individual foods have been tested.

(e) Water, non-iodized salt, and cane sugar are so rarely allergenic that they are not ordinarily tested individually, although they may be so tested. It is usually found that if rice, beef steak, and boiled ham are tolerated, then puffed rice, roast beef, veal, and bacon will be tolerated.

(f) Inasmuch as nearly all individuals with urticaria obtain relief of symptoms within four to twelve hours under this method of treatment, it has been found feasible to add a single new food at each meal so as to provide within a few days a diet possessing satisfactory variety. It is justifiable to prescribe this rapid programme for the majority of patients and to lengthen the intervals between additions of foods only in the occasional case in which longer intervals prove necessary.

Application.—The single food additive diet is applicable to all patients whose urticaria may be due to ingested allergens, and who fall into one of the following groups:—

(1) Those in whom ingested allergens are not clearly evident from the history, the anamnestic approach being a method on which little reliance may be placed.

(2) Those in whom ingested allergens may involve several foods and who cannot be relieved by elimination of only some of these; in such patients multiple-choice elimination diets, food diary, and skin tests (Sulzberger and Rostenberg, 1935; Rinkel, 1944; Rowe, 1934, 1941) would not be effective.

(3) Those in whom cyclic food allergy is present. Cyclic food allergy (Rinkel, 1944) is of three clinical types: (a) the perennial type which is a primary food allergy; (b) the concomitant type which is a food allergy that becomes manifest only when an allergen, for instance, ragweed, is also inhaled, and (c) the thermal type which is not evident until the individual is exposed to cold air or is chilled to, or below, his critical level.

PROCEDURE

In applying the single food additive diet to the patient the following things are done:—

(1) A dietary outline is given the patient, who, we shall assume, is seen in the afternoon, so that he starts with the evening meal.

(2) At each subsequent interview a list of foods already tested is given to the patient, designating those foods which have been tolerated and those apparently not tolerated.

(3) If urticaria develops following any meal, the new food added at that meal is suspected of being an allergen and is not repeated for from five to seven days. If urticaria develops upon re-testing, the food is considered to be a proved causative allergen.

(4) If one of the foods suspected is wheat, corn, eggs, or milk, a list of

foods containing the substance is given to the patient, and all such foods are prohibited until after the seven days' dietary outline is completed, following which the suspected food is re-tested.

(5) All internal medication, including vitamins, is discontinued. If medication is necessary, the medicine is tested as a new ingested substance to be tried individually.

(6) Candy, soft drinks, and liquor are prohibited until they are tested individually.

(7) A saline laxative is prescribed immediately before the start of the prescribed diet.

(8) Pyribenzamine hydrochloride, one 50-mgm. tablet, is given to the patient after the use of the saline laxative and before ingestion of the first meal if urticaria is present at that time.

DIET PROGRAMME

First day:

Office visit during afternoon. Programme initiated.

Evening meal: boiled rice (first food item tested).

Second day:

Breakfast: oatmeal (second) cooked with water.

Lunch: rice if tolerated, broiled beef (third).

Office visit during afternoon.

Evening meal: broiled beef if tolerated, boiled rice, beets (fourth).

Third day:

Breakfast: oatmeal and milk (fifth).

Lunch: milk if tolerated, beets if tolerated, boiled rice, plain gelatin (sixth).

Office visit during afternoon.

Evening meal: plain gelatin if tolerated, broiled beef, rice, beets, white bread (seventh).

Fourth day:

Breakfast: white bread if tolerated, puffed rice if rice is tolerated, milk, banana (eighth).

Lunch: boiled rice and milk, white bread, beets, plain gelatin, boiled ham (ninth).

Office visit during afternoon.

Evening meal: roast beef if beef steak is tolerated, beets, white bread, plain gelatin, peas (tenth).

Fifth day:

Breakfast: banana if tolerated, oatmeal and milk, white bread, butter (eleventh).

Lunch: butter if tolerated, boiled ham if tolerated, white bread, beets, plain gelatin, yellow corn (twelfth).

Office visit during afternoon.

Evening meal: veal chops if beef is tolerated, peas if tolerated, butter, white bread, boiled rice and milk, beets, plain gelatin, tea (thirteenth).

Sixth day:

Breakfast: tea if tolerated, puffed rice, milk, white bread, butter, banana, egg yolk (fourteenth).

Lunch: roast beef, butter, white bread, plain gelatin, beets, tea, boiled or baked white potato (fifteenth).

Office visit during afternoon.

Evening meal: yellow corn if tolerated, white bread, butter, broiled beef steak, tea, boiled rice, milk, peas, plain gelatin, pears (sixteenth).

Seventh day:

Breakfast: bacon if boiled ham is tolerated, white bread, butter, tea, milk, banana, shredded wheat (seventeenth).

Lunch: boiled or baked white potato if tolerated, white bread, butter, tea, corn, peas, beets, plain gelatin, boiled ham, Swiss cheese (eighteenth).

Office visit during afternoon.

Evening meal: pears if tolerated, white bread, butter, veal chops, boiled rice and milk, beets, peas, corn, white potato, plain gelatin, lima beans (nineteenth).

The meals described contain all of the food tested. A food that is followed by urticaria should be omitted from all of the meals thereafter. After the seventh day, the patient has attained a variety of foods proved to be harmless, can subsist on them without urticaria, and has probably become familiar with the process of testing new foods so that he is able to continue alone. The following foods may be tested at successive meals:—orange juice, lettuce, chicken, egg white, lamb chops, coffee, vanilla ice cream, tomato, corn flakes, solid chocolate bar, cola drink, and as many additional foods as may be desired.

Book of instructions.—For the convenience of the patient he is given at the start a booklet of instructions (Sutton and Winston, 1947), with space to record the contents of each meal and the result. The contents of this booklet are shown opposite.

DIFFICULTIES IN INTERPRETATION

Ingested allergens may produce urticaria for anything from four hours to seventy-two hours. Foods tested at subsequent meals would therefore tend to be indicted as allergens when they actually are not. This difficulty does not destroy the validity of the single food additive diet, for it merely increases the number of apparently non-tolerated foods, and the error is corrected when the food is re-tested five to seven days later. The practitioner is placed on the alert for such a possibility when three or four consecutive meals are followed by urticaria. When urticaria follows all meals regardless of the food selected, it is likely that food is not the cause of the urticaria.

Another not uncommon difficulty is to find an individual who is relatively free of urticaria during the day but develops lesions during the night. This suggests the possibility of an allergen that requires longer than four hours to act. Usually, when such patients are carefully followed for three days, the pattern is broken because, with the use of the single food additive diet, the food taken at the noon or evening meal is soon changed to one which is free of allergenic activity. If the nocturnal exacerbation is not stopped, only one new food per day is permitted for three days. If this procedure is not effective, it is probable that food is not the cause of the urticaria.

ADVANTAGES OF THE SINGLE FOOD ADDITIVE DIET

The single food additive diet possesses advantages over skin tests and multiple choice elimination diets. Complete relief of symptoms is obtained within twenty-four hours in nearly all instances, although rarely symptoms may persist for as long as three days. Unlike skin testing, the suspected allergen is tested by the eating of it in the manner in which it is normally encountered. The specific ingested allergen is identified immediately and with precision, avoiding the uncertainty of the multiple-choice elimination

INSTRUCTIONS

1. A single, simple food (not a mixture of foods) is tested by eating it and waiting for 4 hours (or more) to see if it causes trouble.

2. If a food has been tested and found harmless, it may thereafter be eaten right along. Thus, as one tests one food after another, the variety of foods which may be selected for the next meal rapidly increases.

3. If a new food causes trouble, one can tell, because itching, new hives, new redness or new tiny blisters nearly always start within 4 hours after that food is eaten. Such a "flare" will begin to fade in a day or two.

4. When a "flare" follows the eating of a food, that food is considered to be "doubtful." It is not eaten again until the physician requests a retesting of it. During the flare and until the flare shows definite fading, one eats nothing new but continues to eat the previously tested harmless foods. When the flare fades, one starts testing new foods again, one after another.

5. It is necessary to keep records, written, careful and up to date, showing (a) the day of the month, (b) the food eaten on that day, (c) the meal at which they were eaten (breakfast, lunch, dinner), and (d) the itchiness after each meal ("flare" or "no flare"). At each mealtime make entries on pages 2 to 14, provided for the purpose.

6. It is necessary to keep records, written, careful and up to date, showing the results of the tests, listing (a) tolerated foods, (b) doubtful foods as judged by first testing, and (c) harmful foods as proven so by retesting. Make entries on pages 15 and 16, provided for the purpose.

7. It is necessary to adhere strictly to the plan. Do not confuse the effort by chewing gum, eating candy or drinking pop or other drinks which are not being specifically tested. Do not take any medicine unless the doctor supervising your elimination diet approves the medicine.

DIRECTIONS FOR EACH DAY

First Day: The diet is prescribed and explained. Take the prescribed laxative and other medication as ordered. You may ingest water, noniodized salt and sugar from the start. When testing a food, there is no limit as to quantity.

A POSSIBLE DIET LIST				
DAY	DATE	BREAKFAST	LUNCH	DINNER
1				rice
2		oatmeal	beef	beets
3		milk	gelatin	bread
4		banana	boiled ham	peas
5		butter	corn	tea
6		egg	white potatoes	pears
7		corn flakes	swiss cheese	chicken
8		orange	celery	lima beans
9		coffee	lettuce	milk chocolate
10		grapefruit	asparagus	string beans

THE DIET ACTUALLY PRESCRIBED				
DAY	DATE	BREAKFAST	LUNCH	DINNER
1				
2				
3				
4				
5				
6				
7				
8				
9				
10				
11				
12				
13				
14				
15				
16				
17				
18				
19				
20				

Page 1

DATE	FOODS EATEN	FLARE
	BREAKFAST	
	LUNCH	
	DINNER	
	BEEAKFAST	
	LUNCH	
	DINNER	

Page 2

RESULTS OF TESTS

TOLERATED FOODS Eat with any trial	DOUBTFUL FOODS	FOODS PROVED BAD WHEN TESTED
Water Noniodized Salt White gran- ulated cane sugar		

diets, which are in fact extremely difficult of execution. Conversely, ingesta that are suspected of being allergens but are not such, are clearly demonstrated to be non-allergenic. The time required for identification of the ingested allergens is short in contrast to the use of the multiple-choice elimination diets. The presence of cyclic food allergy is determined more readily with the single food additive diet than with the multiple-choice elimination diets because there are fewer variable factors in the former. Skin tests are of no value in cyclic allergy (Rinkel, 1944).

ILLUSTRATIVE CASES

Case 1.—C.K., aged fifty-three, saleslady, was seen February 10, 1947, with urticaria of five months' duration. Previous unsuccessful measures included the use of pyribenzamine hydrochloride and dihydrotachysterol, and the extraction of infected teeth. She was placed on the single food additive diet for the detection of ingested allergens, and within five days she was free of urticarial wheals and was eating a variety of foods. Upon initial testing she developed urticaria following milk, apples, peas, peaches, prunes, chicken, hominy, kraut, grapefruit, and chloretone spray for the throat. Upon re-testing she tolerated all suspected items except peas, milk, and chloretone spray. December 1947, fifteen months from the onset of her urticaria, ingestion of peas was still productive of urticarial wheals.

Case 2.—J. L., aged forty-seven, housewife, was seen March 21, 1947, with urticaria of four months' duration. She had taken no internal medication except vitamin capsules. Examination revealed scattered urticarial wheals without evidence of scabies or other parasitic infections. She was placed on the single food diet for the detection of ingested allergens on March 21, 1947. Within twenty-four hours she was free of wheals. Ingestion of butter was followed by urticaria within an hour. She was not permitted to use butter, and the process of testing was continued, but no other allergen was discovered, and she remained free of urticaria.

SUMMARY

A method of detecting ingested allergens productive of urticaria is presented which provides relief of urticaria due to ingested allergens in many instances within four hours, and in all cases within a few days. The patient does not starve and does not suffer nutritional deficiency. The method demonstrates the specific ingested allergens productive of urticaria accurately, quickly, and simply, as contrasted with the use of skin tests and multiple choice elimination diets, and lends itself to use by the general practitioner.

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SOME COMMON INDUSTRIAL DISEASES OF THE SKIN

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To the general practitioner, the industrial medical officer and the dermatologist, the problems of the etiology, therapy and prevention of occupational dermatitis are becoming of increasing complexity. Not only do potential irritants multiply, but resulting skin manifestations become less easy to classify. Changes in age, sex, and physical types of employee, and the dietetic controls of to-day produce a confused picture—a varied “soil” may have produced an unusual “weed”. A further factor, often overlooked, is to be found in the use, at every social level, of modified cleansing agents, not only at work but in the home. The detergent problem covers a wider field than is generally envisaged and it may be of interest to discuss two main aspects of occupational disease:—(a) Irritative reaction to cleansing agents; (b) irritative reaction to lubricants with reference to the methods adopted in their removal.

The human skin in health is a mosaic of firmly adherent, yet elastic cells of high resistive capacity to friction, pressure, chemical and bacterial irritants. Considerable reactive and reproductive capacity exists. In health the skin is covered with a finely divided oil-in-water emulsion of acid reaction. Its surface is supplied with aqueous and oil secretion from sweat and oil glands, and is penetrated by hair follicles. Its thickness varies. The pH index in different anatomical areas and in different individuals is inconstant. Resistive capacity differs according to the terrain subject to contact, and thus inflammatory reactions may be found to a widely applied noxa over certain areas only. Broad and basic principles of reaction between skin and potential irritant are, however, universally applicable.

DERMATITIS DUE TO CLEANSING AGENTS

“Occupational” dermatitis due to cleansing agents may follow directly on the irritative effect of physical or chemical contact during the course of employment. But it may equally follow the use of agents provided for removal of stain (or other contaminant) soiling the worker’s hands. Analogous reactions follow exposure to the many and widely advertised products supplied by the grocer to the harassed and ill-supplied household worker or mother for use in her kitchen, bathroom or nursery. Too often a mutually irritative influence is exercised. A wage earner’s eruption may be of double origin—to the irritant at work is added a secondary irritant in the home. An attempt is made in the first section of this article to outline several causative factors and to show how such contacts induce inflammatory change.

Cleansing processes form an integral part of industry; many different types of contaminant demand removal and, since the chemical and physical types thereof are protean, so the substances employed to such purpose are necessarily variable. Resulting skin reactions are, in contrast, of a common type. Differential diagnosis as to the exact irritative and inflammatory agents responsible, determined by inspection of the injured tissue, is rarely possible. The degree, distribution, and time elements are equally inconstant, since the personal factor confuses the picture. In general, a knowledge of the activity of contacts at work combined with the history and distribution is sufficient to decide between constitutional and occupational influences.

Occupational disturbance of the skin occurs solely on the portion of skin exposed in its early stages. Secondary phenomena on non-exposed areas may follow. Flexural "eczema", for example, may follow the use of soap on the hands, but only occurs when those areas have been severely inflamed. Reaction on popliteal, antecubital and facial areas may follow absorption rather than direct contact. An œdema and erythema confined to the eyelids as the primary manifestation will occur only if these areas are contacted by air-borne irritant. It will not be found if the hands alone are exposed to a suspected chemical and remain unaffected.

It may be accepted as a fundamental principle that the more efficient a cleansing agent be in industry or in the household, the more rapid the capacity of a chemical to take a stain from a tablecloth, dirty oil from a mechanical component, dye from a workman's hand, or grease from a household dinner plate, then the greater will be the keratin or fat solvent action exercised on the skin of the worker. Sooner or later the latter may be expected to develop inflammatory change in his epidermis.

Dermatitis due to agents employed at, or subsequent to, employment.—Eruptions on the hands from "occupational" cleansing agents are induced by one of four factors:—(1) Fat solvent irritation; (2) Keratin solvent irritation; (3) Abrasive irritation; (4) Allergic response.

Allergic response is too controversial a subject to be included in this article and only brief reference is made thereto. Its discussion must be left to detailed investigation of particular problems. In any event the proportion of idiosyncratic dermatoses among the many cases of industrial dermatitis from cleansing agents and soaps is very small indeed. A true idiosyncratic response to soap and to cleansing agents is probably rare; such reaction to be proved must manifest itself if contact is in so small a degree that it could not be envisaged as following exposure thereto in individuals of a normal type. It is perhaps only found in persons of an allergic background and its existence can only be determined by positive patch tests of colouring matter, scent or adjuvant. In practical control of occupational dermatitis its existence is merely a matter of dermatological interest rather than one of necessary investigation.

FAT SOLVENT IRRITATION

Dry cleaning workers utilize fat solvent agents as distinct from the cleansing

agents which remove grease physically: they de-fat soiled garments and act in a similar manner to the materials employed in removing paraffin and oil covering mechanical parts in the engineering industry. For example, workers in the dry cleaning industry utilize alcohols, carbon tetrachloride, and soaps for immersion of used and worn articles of clothing in revolving drums. After such processing these are normally removed for ventilation with circulating air. Transient manual contact may be sufficient to induce tissue reaction, but more frequently hand cleaning for delicate articles is essential, and the resulting dermatitis is the more easily induced. Dry eczematous reaction on fingers, wrists and dorsal areas of the hand with inflammation of interdigital areas, in particular with added perionychia, results. The skin tends to split, and becomes harsh to the touch because its natural fats are removed. A proportion of workers also develop a localized pompholyx. Aqueous solutions are often employed in the form of ammonia, caustic soda and potash, and they, like the active detergent soaps, exercise a powerful local irritative reaction because of their *keratin solvent* action. Both agents are mutually aggressive.

Painters.—Benzene is widely used, as are its allied hydrocarbon compounds, as diluents for varnishes, paints, and polishes. This agent and its substitutes act as irritants on every type of skin, even if only employed for cleansing of the worker's hands, and provide a common cause of occupational dermatitis.

Metal cleansing.—Apart from abrasives used in the polishing of partially finished articles, a number of organic solvents are employed for cleaning off accumulated oil and debris from both small and large metal components. One of the most commonly employed agents is trichlorethylene; its degreasing efficiency renders it highly potent in de-fatting, and therefore in inflaming, the human skin. A mutually aggravating effect of mechanically irritative particles and of removal of natural skin oils is exercised.

"Alkali" cleaning.—Perhaps one of the most active factors in producing dermatitis in men and women employed as canteen workers, office cleaners, lavatory attendants, and in heavy domestic work lies in the alkali content of many cheaper, although highly efficient, soaps. Consideration of the fat solvent, abrasive and macerating effects of these is obvious to every medical man in factory and panel practice alike. The so-called "soft soaps" and the constant immersion in a fluid of highly detergent and degreasing capacity provide a highly potent agent in inducing occupational dermatitis. The all embracing diagnosis of "housewife's eczema" is common in every dermatological out-patient department.

A simple example of "mixed" causation is to be found in the eruptions of the hands found in "bakers' assistants"—too often flour is blamed; too rarely is consideration given to the irritative results of bench scrubbing, degreasing of tins and constant application of alkaline soaps undertaken as part of the week's routine duties, and to the insufficient supply of dry, apart from clean, towels in the workplace. Then there is the housewife who,

working by day gainfully, uses active agents in her home which exacerbate injuries encountered during employment.

Macerative effects.—Constant immersion of the hands in water, even if uncontaminated by irritative contact, tends to produce deleterious change. Too often the skin becomes sodden and the cuticles are loosened from the nail. An entry for bacterial invasion is offered. The tissues become less resistant to hitherto innocuous personal and household cleansing agents, since physical harm readily induces easier penetration of chemical irritant into the epidermis. Rarely will bacteria penetrate between nail and cuticle on the average healthy hand, but if such cuticle is lifted away from the nail many organisms—staphylococci, moulds, and fungi—are offered an open door. A cook in a canteen peeling potatoes, cleaning carrots and cabbages, and washing celery, rarely develops epidermal sensitivity to the vegetable contacts, but her fingers may rapidly accept a staphylococcal invasion because her water contact lifts her cuticles from their firm attachment to the nail, and allows infection to follow. Similarly, a skin sodden, split and broken provides but a poor barrier to bacteria, as contrasted with the toughened firm integument provided by nature.

To the thoughtful dermatologist it appears a miracle that the skin of the surgeon, and of the nurse, survives the vicious attacks which each are trained to make upon their skin as part of their daily ritual. It is a matter for further astonishment that nature can resist and later repair the attacks of the many utensil abrasives so freely offered to the housewife. Healthy and reasonably aseptic skin is subjected to traumatic scrubbing, macerative soaking, and chemical application which decrease and abrade. Yet dermatitis is only to be found in a small proportion of men- and women-kind. The impermeable covering with rubber gloves offers some solution, but there is still a lack of consideration for the natural nutritive and protective oils of the skin. Yet the surgeon, the theatre sister, and the householder survive superficially.

ALTERNATIVE CLEANSING AGENTS

The past decade has seen an intensive research into the development of non-degreasing, non-irritative cleansing agents used in the home, the hospital and the factory. The need for such agents is recognized, and the answer largely supplied by commercial organizations has been freely offered. Soaps can be regarded as lowering the interfacial tension between the cleansing agent (water) and the oil and "soil" of the contaminated tissue. Emulsification takes place and the cleansing solution "wets" or surrounds the grease, oil and solid particles of dirt. Mechanical action aids removal by rinsing effect. Lathering plus abrasive action, although highly effective, is potentially injurious. To avoid this last effect organic compounds have been introduced. These are usually "sulphonates" or "sulphates" and act chiefly as emulsifying agents. They do not alkalyze the skin, and used in low dilution appear to exercise a less degreasing effect. If suitably balanced they

can leave the skin clean, and not remove the "oil in water" and "acid" mantle on the epidermis which healthy skin must possess. They are less likely to produce insoluble calcium salts (e.g. calcium oleate) and interfere but little with secretory activity. They also leave some degree of resistive power towards skin invaders (bacteria, virus and mycotic). They cleanse more easily and therefore reduce the demand for an injurious friction on the horny layer.

DERMATITIS DUE TO OIL

Dermatitis due to oil is one of the most common problems of industrial disease. Its causes may be conveniently subdivided into three main groups, although sharp differentiation is not always possible concerning the mechanism whereby the eruptions are induced. Frequently causation is of multiple origin. Lubricants may be of animal, vegetable or mineral origin. Combinations of all three, often with added aqueous diluents, are employed. Each separately, or all conjointly, may induce pathological response in the skin.

The *first group* of disturbances, commonly referred to as *oil boil*, or *oil acne*, or *oil grubs*, are in part obstructive and due to mechanical blockage of the hair follicles and sebaceous ducts, and in part due to an irritative effect of the lubricant on the epidermis which induces a hyperkeratotic response by the cells lining the mouth of the sebaceous ducts. The clinical manifestation is an evenly distributed but diffuse development of "black-heads" over the area primarily exposed to the lubricant. A rapid secondary infection by staphylococci is a constant feature and may mask the primary lesion. The forearms, especially the posterior aspect, are covered with comedones of varied severity and size; the legs, chiefly on the anterior aspect of the thighs, become similarly involved. Trousers and under-garments, being heavily impregnated with oil, spread the eruption. Infrequent change of clothing and insufficient washing of the skin exacerbate the disturbance. It is of interest to note that a similar reaction is often seen when clean paraffin or vegetable oils are employed for cleaning or sedative purposes for infants, or on the sunburned skin of adults. Incompletely cleansed towels, rags and waste materials supplied for use after work, may spread bacteria. There is also evidence that the lubricant itself may be contaminated bacteriologically and a lessened spread of infection may follow the incorporation of antiseptics in the oil.

The *second group* of disturbances due to oil lubricants is that found with increasing severity as a result of the use of "oil-water" emulsions. These are employed when a cooling as well as a lubricant effect is desired in high speed cutting or shaving machines. These emulsions, known in industry as "mystic", "suds", "coolant", exercise a doubly irritative effect on the human skin. Such emulsions are rendered stable by the addition to the oil and water mixture of emulgents. The constitution of these varies, but their purpose is common. Their potential irritative effect on the skin is twofold.

working by day gainfully, uses active agents in her home which exacerbate injuries encountered during employment.

Macerative effects.—Constant immersion of the hands in water, even if uncontaminated by irritative contact, tends to produce deleterious change. Too often the skin becomes sodden and the cuticles are loosened from the nail. An entry for bacterial invasion is offered. The tissues become less resistant to hitherto innocuous personal and household cleansing agents, since physical harm readily induces easier penetration of chemical irritant into the epidermis. Rarely will bacteria penetrate between nail and cuticle on the average healthy hand, but if such cuticle is lifted away from the nail many organisms—staphylococci, moulds, and fungi—are offered an open door. A cook in a canteen peeling potatoes, cleaning carrots and cabbages, and washing celery, rarely develops epidermal sensitivity to the vegetable contacts, but her fingers may rapidly accept a staphylococcal invasion because her water contact lifts her cuticles from their firm attachment to the nail, and allows infection to follow. Similarly, a skin sodden, split and broken provides but a poor barrier to bacteria, as contrasted with the toughened firm integument provided by nature.

To the thoughtful dermatologist it appears a miracle that the skin of the surgeon, and of the nurse, survives the vicious attacks which each are trained to make upon their skin as part of their daily ritual. It is a matter for further astonishment that nature can resist and later repair the attacks of the many utensil abrasives so freely offered to the housewife. Healthy and reasonably aseptic skin is subjected to traumatic scrubbing, macerative soaking, and chemical application which decrease and abrade. Yet dermatitis is only to be found in a small proportion of men- and women-kind. The impermeable covering with rubber gloves offers some solution, but there is still a lack of consideration for the natural nutritive and protective oils of the skin. Yet the surgeon, the theatre sister, and the householder survive superficially.

ALTERNATIVE CLEANSING AGENTS

The past decade has seen an intensive research into the development of non-degreasing, non-irritative cleansing agents used in the home, the hospital and the factory. The need for such agents is recognized, and the answer largely supplied by commercial organizations has been freely offered. Soaps can be regarded as lowering the interfacial tension between the cleansing agent (water) and the oil and "soil" of the contaminated tissue. Emulsification takes place and the cleansing solution "wets" or surrounds the grease, oil and solid particles of dirt. Mechanical action aids removal by rinsing effect. Lathering plus abrasive action, although highly effective, is potentially injurious. To avoid this last effect organic compounds have been introduced. These are usually "sulphonates" or "sulphates" and act chiefly as emulsifying agents. They do not alkalize the skin, and used in low dilution appear to exercise a less degreasing effect. If suitably balanced they

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EPIDERMOPHYTOSIS AND THE DERMOPHYTIDES

Epidermophyton infections of the feet are by far the most common type of mycotic infection met with in practice. Of 871 young men entering the U.S. Naval Academy, 60 per cent. were found to have fungus infection of the feet. Of these, only 46 per cent. were aware of the infection (Broyles, 1945). The infection tends to be localized and chronic in the colder part of the year with seasonal exacerbations in the hot summer months. The year 1947 was characterized by the large number of patients attending clinics during the hot, dry summer and autumn for treatment of fungus infections. The majority complained, not of their feet, but of "dermatitis" of the hands.

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Infection is acquired commonly from infected bath mats, wooden or concrete floors of changing rooms in sports clubs, and swimming baths, bath houses, pit-head baths and the sea shore. Inquiry often reveals some change in the patient's habits—a holiday, change of lodgings, or seasonal sporting activity. "Athlete's foot" is a well-earned term, for adolescents and young adults are predominantly affected, men more than women. The disease is rare in childhood and old age.

The fungus mycelium grows in the dead horny layers of the epithelium, sites of election being the fourth interdigital cleft and the arch of the foot. These areas are subject to the secretion of a profuse alkaline sweat which macerates the thick horny layer and provides an ideal culture medium for the mycelium, incubated in the warmth and dark provided by the shoes. Hyperhidrotics are therefore particularly prone to fungus infection. The sweating is often due to flat feet, or the wearing of heavy, ill-fitting boots, but may be psychogenic in origin.

Circulatory stasis due to varicose veins or vasomotor disturbances is important in some cases. Carbohydrate metabolism disorder, ranging from

The "cutting oils" in question may cause dermatitis of the oil boil type, by the penetration of the oil content into the sebaceous ducts, or they may irritate idiosyncratically, but more often their deleterious effect is solely due to the emulgent. Such effect is due to the emulgent remaining on the skin at the end of a period of work, rendering the epidermis more susceptible to the detergent effect of soap subsequently used for cleansing the hands and arms. The natural fats of the skin are extracted by soap and hot water to too great a degree, and the worker is left with a dry skin which gradually becomes cracked, ill-nourished and infected. Such change occurs in spite of the fact that it has been apparently well "lubricated" at work. Research during the war, when women of all ages and types were employed working with oils, and using oil-water emulsions, tended to show that workers with a fine, dry and delicate skin were more prone to develop "mystic" dermatitis than those with a thick and naturally oily, tough skin. As a contrast, those of the latter class appeared more liable to develop oil acne and oil boils than those of the previous class, who reacted abnormally to the "coolant" contacts. The picture may perhaps be a little confused by the fact that a skin dried and fissured by emulsifying agents is the more easily penetrated by bacteria and therefore may develop local sepsis of the staphylococcal type. The age factor deserves attention in that the "youthful" oily skin (as contrasted with the "senile" atrophic skin of the elderly employees) may react to produce blackheads and pustules after exposure to either type of lubricant. The older worker on the other hand develops more easily the superficially desquamating type of dermatitis with irritation and erythema.

The *third group* of dermatitis cases resulting from exposure to oils is found in those workers who appear to develop idiosyncratic response to lubricants. Such local allergy is in my opinion rare towards mineral oils, but rather more common to the extracted oils of vegetable origin. The personal factor is predominant, and forecast as to liability to outbreak cannot be made, Patch testing alone may appear to offer some solution, but patch testing is a transient procedure and neglects the factors of friction and of cleaning. Discussion of this problem with workers tends to suggest that immunity will often develop and certain contacts in the first few weeks will induce local discomfort; the skin may later become tougher and more resistant.

CONCLUSION

Choice of employee for particular contacts, care as to cleansing procedure at the end of a day's work, early diagnosis of irritative response and considered thought as to the methods whereby contacts irritate may give some degree of solution of the many problems involved in occupational dermatitis, but it is likely that progress in chemical efficiency of materials handled tends to induce an increase in epidermal reaction.

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Circulatory stasis due to varicose veins or vasomotor disturbances is important in some cases. Carbohydrate metabolism disorder, ranging from

glucose intolerance to frank diabetes mellitus, is often found if looked for. Patients known to be liable to fungus infections do well to avoid excess carbohydrate and alcoholic consumption. Allergic factors are potent, as is shown by the flares following contact with external irritants or the ingestion of food allergens or during intercurrent infections.

Shoes and socks are readily contaminated and the lending of sports gear at schools and clubs cannot be too strongly condemned.

Signs and symptoms are variable and often absent. There may be slight irritation between the toes when the feet are warm. Cracks and fissures between the toes often become infected with pyococcal organisms, with resultant local inflammation and lymphangitis. The common chronic form is limited to the cleft between the fourth and fifth toes, often of one foot only. The epithelium is thickened and macerated, it peels away to reveal a red and weeping under-surface which may show deep fissures.

The disease tends to spread into the thick moist horny layer of the sole rather than the more delicate epithelium on the dorsum of the foot and thus contrasts with the pyogenic infections. Isolated chronic patches are often seen in the arch of the sole and below the medial malleolus. There is well-defined erythema with an undermined scaling edge and, often, scattered over the patch are deep vesicles and pustules. Sometimes the fungus characteristic, a ring of vesicles at the extending edge, is seen with a tendency to central healing. The infection tends to be asymmetrical, one foot only or predominantly being affected. The vesicles contain clear glycerin-like fluid.

An unusual chronic form due to *Tinea rubrum* presents as a diffuse scaling erythema with considerable hyperkeratosis of the whole sole. The erythematous area is often sharply demarcated from the normal skin. With the onset of the hot weather, a new infection or other irritant, the lesions become acute. New tense vesicles and pustules form and the scaling edge extends rapidly leaving an oozing raw surface behind it.

After a period varying from two weeks to some months, dermatophytide phenomena may occur. Vesicles and bullæ erupt on the sole of the unaffected foot, on the palms and on the palmar surface and sides of the fingers. The eruption is accompanied by intense irritation. The more superficial vesicles burst, leaving a weeping surface, but the deeper ones tend to dry, forming brownish scales.

Clinically, the resemblance to some types of contact dermatitis is close, especially if irritated by the application of strong fungicides. Contact dermatitis usually presents as superficial, closely set vesicles, mainly in the dorsum of the hands and fingers. Erythema is more marked, the vesicles are more readily destroyed, and new crops follow further exposure to irritants, whereas the dermatophytide crops occur regularly.

The eruption is often confused with dysidrosis or pompholyx, which occurs in over-anxious, debilitated persons and is not seasonal. Dermophytides occur only in the presence of an active focus of fungus infection,

and result from the absorption and circulation of the products of the fungus metabolism, the eczematous reaction occurring when a sensitized area of skin is reached.

Fungus mycelium cannot be demonstrated by examination or culture in the secondary lesions, therefore fungicides can only be harmful irritants to an acute process. A similar reaction can be produced in patients sensitized by a past fungus infection, by injections of trichophytin. No great specificity for fungus types is claimed in this reaction. In the presence of an active fungus infection the reaction may be negative. Other dermatophytide reactions include eczematous patches on the legs below the knees and a generalized follicular lichenoid eruption.

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Epidermophyton infections of the hand do occur but are rare in Great Britain. The diagnosis should never be made unless fungus mycelium can be demonstrated in the lesions.

Differential diagnosis.—Dysidrosis or pompholyx. Contact dermatitis. Eczema. Pyococcal infections, pustular psoriasis and bacterid, the *dermatitis repens* of Crocker. Psoriasis vulgaris and erythema multiforme. Tertiary syphilis.

Most practitioners rely on the clinical appearance with confirmation by microscopy. Accurate results are obtained by culture when facilities are available. Microscopic examination for mycelium is the most important investigation. If repeated examinations are negative the clinical diagnosis should be reconsidered. Little equipment is required for the examination other than a microscope; the procedure is simple and consumes little time. It will prevent many diagnostic errors, and therefore therapy will be more rapid and efficient.

From the growing edge of the lesions scales are scraped with a scalpel on to a clean slide; vesicle tops are removed with fine scissors and inverted in 10 per cent. caustic potash under a cover slip. Scrapings of intertriginous debris are unsatisfactory; every effort should be made to obtain epithelium from the most recent part of the lesion. The slide is then gently warmed and left for several hours ringed with petroleum jelly to prevent evaporation and crystallization. The cover slip is pressed down to thin the macerated epithelium and search is made under low power with reduced illumination.

True fungus mycelium is slightly tinted, often septate, exhibits true branching and ramifies among the colourless squames of epithelial cells, often interrupted by, or terminating in spores. Squame edges should not be confused with mycelium, being colourless, ill-defined, too numerous and irregular; examination of the thin edge will usually resolve any doubt. Mosaic fungus, now thought to be cholesterol crystals, crosses the field more regularly than true mycelium. Fat globules may simulate spores, and caustic potash crystals and cotton-wool fibres may cause difficulty; the length, size and definition, the lack of substance and branching in the latter are characteristic. The appearance should be confirmed under high power with full illumination.

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Prophylaxis.—(1) Avoidance of exposure by wearing bathing shoes. Bathing the feet in 1 per cent. hypophosphite solution before and after swimming and in bath houses is not a particularly effective measure.

(2) Prevention of infection in those especially liable. Daily soaks in 1 in 4000 potassium permanganate solution for five minutes reduces hyperhidrosis. Powdering both shoes and socks with 5 per cent. propionic acid—propionate or undecylenic acid—undecylate in salicylic acid powder.

(3) Detection and adequate treatment of infected persons.

TREATMENT

The fatty acid fungicides.—It has long been recognized that the skin protects itself by its "acid mantle". Where the skin secretions cannot evaporate freely, as in the toe clefts, the usually high acidity (pH 4-5 approx.) is reduced to the neutral or alkaline side (pH 6.5-6.8 or higher). Many fungicides of long-established value, e.g. Whitfield's ointment, have a high acid content. Propionic, undecylenic and caprylic acids were all shown to be excellent fungicides *in vitro* (Peck and Rosenfeld, 1938). Clinical trials confirmed their efficiency (Keeny *et al.*, 1944). The main advantages over other fungicides are their low irritant and sensitizing properties. Although ideal for mass treatment and prophylaxis, better results are obtained in combination with the well-established remedies (Sulzberger *et al.*, 1946). At present these preparations are difficult to obtain in this country and bases of the eucerin type may be substituted for the more complicated formulæ. The method of attack depends upon the type and stage of the lesion.

(1) *The acute stage.*—In this phase there is often a secondary pyogenic infection and lymphangitis for which sulphonamides by mouth and penicillin by injection may be necessary. Local treatment is limited to soaks twice daily for ten minutes in 1 in 4000 potassium permanganate solution, followed by the application of a fatty acid preparation such as:—

Undecylenic acid	5
Zinc undecylenate	15
Liquid paraffin	5
Collone S.E.	q.s.
Water.....	to 100

The application of strong keratolytic fungicides in the acute or subacute stages can only do harm.

(2) *The subacute stage.*—The stage of vesicular weeping lesions. Byrne (1947) had good results with a modern mercurial preparation:—

Phenyl mercuric chloride, 0.5 per cent., precipitated on calamine	15 grains (1 gm.)
Zinc oxide	30 grains (2 gm.)
Glycerin	30 minims (1.8 c.cm.)
Distilled water.....	to 1 oz. (28.4 c.cm.)

The lotion should be applied as frequent wet dressings for a few days. Rapid improvement with drying of the patches results. If large granulating areas are present a fatty acid preparation is preferable, for sensitization

reactions may occur with the mercurial lotion. A single dose of X-rays, unfiltered, is often helpful to render the lesion quiescent.

When the lesions are dry 0.125 per cent. phenyl mercuric chloride dissolved in distilled water and incorporated in a eucerin base can be substituted (Byrne, 1947).

(3) *Chronic desquamating lesions*.—Here the principle is to strip off the horny layers of the epidermis, thus removing the culture medium of the mycelium. This is best accomplished by the use of Whitfield's lotion, twice daily for a week.

Benzoic acid	180 minims (10.5 c.cm.)
Salicylic acid	120 minims (7 c.cm.)
Acetone	2 oz. (57 c.cm.)
S.V.M.I. to	8 oz. (227 c.cm.)

Followed by applications of Whitfield's ointment for a further week. The process may be repeated with advantage on very horny feet.

The exposed mycelium may now be attacked with a mercurial preparation or a fatty acid preparation. Peck and Russ (1947) used:—

Sodium propionate	12.3
Propionic acid	2.7
Sodium caprylate	10
Ointment base to	100

Castellani's carbolfuchsin paint is another useful, if messy, remedy.

Fewer relapses occur if therapy is continued for some weeks after clinical signs are absent.

Dermophytides.—Soap and water should be avoided, liquid paraffin or arachis oil being substituted. Local applications of 2 per cent. collosol ichthyol in zinc cream are useful. Small doses of X-rays, 1000 unfiltered, repeated in two and four weeks, help in healing the lesions and preventing unpleasant exacerbations during the treatment of the original focus.

Dermophytides clear spontaneously after eradication of the original focus; strong fungicides are contraindicated.

Prevention of reinfection.—Contaminated bath mats and socks should either be boiled in soapy water or soaked in 10 per cent. formalin solution or in 1 in 20,000 aqueous phenyl mercuric chloride, before washing. During treatment, cheap cotton socks should be worn, which can later be discarded and burnt. Boots and shoes should be exposed to formalin vapour in a closed container for twenty-four hours or swabbed with 10 per cent. formalin solution and exposed to the air for twenty-four hours before wearing. Shoes and socks should be freely powdered with a fungicide for months.

TINEA CIRCINATA

This is now a relatively uncommon affection of the extremities occurring mainly in children and those in contact with animals. Small spore endothrix (human) trichophytons are rarely seen and lesions are minimal. Large spore

ectothrix (animal) trichophytons are the usual causal agents. Infection is commonly contracted from affected puppies, kittens, ponies and calves.

Signs and symptoms.—In its mildest form a pinkish scaling papule is seen which spreads peripherally and clears at the centre. The margin shows scaling and sometimes small vesicles. The lesions tend to die out before reaching any considerable size. Mild irritation is common. The more severe forms have a ring of pustules and vesicles at the extending margin, which is red and raised. Polycyclic rings are often seen due to fusion of lesions. The rings are larger and persist longer than in the mild type.

Deep pustular ringworm, or kerion, is usually contracted from cattle (*Trichophyton discoides*). An infiltrated plaque develops, one or two inches in diameter, the surface studded with deep pustules. Secondary pyogenic infection with lymphangitis is common. Ring formation and peripheral spread are unusual, the severe inflammatory reaction subsiding in three or four weeks with considerable scarring. Several relapses may occur before healing is complete. At the height of the inflammation the plaque is swollen, red and boggy, suggesting the presence of deep pus; this is not to be found in any quantity and no incision should be made.

Diagnosis.—Mycelium can be demonstrated in scales, vesicle tops or hairs from the affected areas.

Treatment.—*Tinea circinata* responds readily to treatment with strong fungicides, Whitfield's ointment being as good as any. Chrysarobin 1 per cent. in Lassar's paste and strong tincture of iodine are also satisfactory remedies.

The kerion type requires frequent hot wet dressings with 1 in 2000 mercury perchloride in normal saline, or 1 in 4000 potassium permanganate. For severe infections X-rays, 100r repeated in two weeks' time, accelerate healing and soothe the inflammation.

ONYCHOMYCOSIS

This infection is chronic and difficult to clear with any method of treatment. The lesions are unsightly and therefore occasion distress to patients. Spread occurs from such a chronic focus to the surrounding skin and to other nails.

Pathology.—Both epidermophyton and trichophyton groups may be responsible; monilia is rarely found except as a secondary contaminant. *Trichophyton rubrum* causes a particularly chronic and resistant onychomycosis.

Signs and symptoms.—At first only one or two nails are affected. The invasion occurs from the free edge or from the lateral nail fold, unlike any other form of nail affection. The nail becomes opaque, brownish or green, thickened, distorted, ridged and friable. The nail is often lifted away from the nail bed, which scales profusely. The free edge is broken, irregular and crumbling, owing to the friability of the affected portion; eventually the nail is considerably shortened.

Diagnosis.—The condition must be distinguished from congenital deformity, eczema, psoriasis, lichen planus, chronic paronychia, and trauma of the nail fold. The asymmetry, few nails initially involved, late onset, absence of lesions other than mycotic ones elsewhere, and the typical mode of onset are helpful points.

Fungus mycelium is difficult to demonstrate in the nail. The scrapings taken from the deeper part allowed to soak for twenty-four hours in 20 per cent. caustic potash are most likely to give positive results. Culture is more satisfactory.

Treatment.—Satisfactory results are difficult to obtain. If several nails are involved complete removal under local or general anæsthesia is the best method. The nail bed and fold are thoroughly scraped with a scalpel to remove all infected tissue. This is followed by painting with 5 per cent. chrysarobin in spirit and acetone, equal parts. The painting is continued until the nail is completely grown. With all precautions a small percentage will be unsuccessful.

For single or partially affected nails, if radical treatment is refused, the friable portion is scraped away daily. This can be done with a scalpel, glass paper or a dental burr. Scrapings should be burnt. Strong fungicides—Whitfield's ointment, chysarobin or a fatty acid preparation—are then applied. The procedure is repeated until a satisfactory nail grows. X-rays and thorium-X are poor fungicides and can be of little use in this condition.

MONILIA INFECTIONS

Yeast organisms are present in 70 to 80 per cent. of normal skins (Cornbleet, 1924). *Monilia alba* is rarely found except in pathological lesions. These occur in debilitated children or in adults whose hands and feet are constantly wet, particularly with sugar-containing fluids. Housewives, bar tenders, fruit and vegetable packers are chiefly affected. Obesity and carbohydrate metabolism disturbances are important factors.

(1) *Erosio interdigitale blastomycetica*

The fourth interdigital space is the usual site; infection spreads to the other finger clefts later. Intertriginous lesions of the feet usually affect all the interdigital spaces. The patients are often diabetics or hyperhidrotics.

Signs and symptoms.—The initial lesion is a small papule or vesicle which extends peripherally but spares the dorsum of the hand. The overlying horny layer is thickened and boggy, resembling damp white blotting-paper. As it peels away it leaves a circinate area of bright red, moist epithelium. The edges are deeply undermined and small vesicles are occasionally seen. At the base of the clefts deep fissures may be present. Cutaneous moniliasis may resemble psoriasis closely, the parakeratosis psoriasisforme of Darier. The condition is very chronic and symptoms are often slight, unless a secondary pyogenic infection occurs.

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THE PRESENT STATUS OF THE SEX HORMONES IN DERMATOLOGY

By DAVID I. WILLIAMS, M.B., M.R.C.P.

Assistant Physician, Skin Department, King's College Hospital; Dermatologist, Bolingbroke Hospital; Consultant in Dermatology, Essex County Council.

THE subject of the present status of the sex hormones in dermatology is one that must be approached with some hesitation and diffidence. The obvious association between condition and texture of the skin as well as certain specific conditions of the skin with these hormones should by now have led, it might be thought, to clear-cut indications for their use; so far from that being the case the story, with few exceptions, is one of increasing confusion and bewilderment. The literature on the subject, both from the clinical and experimental points of view, is vast and conflicting to a degree, one worker's dogmatic assertion being contradicted by the next, and clinical trials have only too often been on few cases and these inadequately controlled. The reason for the confusion is, of course, not far to seek. Endocrinology is a subject of intriguing but bewildering perplexity; the interrelationship of the glands, their mode of action, their linkage with the autonomic nervous system, the continual isolation of new hormones, the effect of vitamin deficiencies, the problem of anti-hormones, the varying susceptibility of different tissues, all serve to make increasingly difficult a line of treatment which in its early days seemed to promise easy success. However, the laboratory workers, by intensive and often brilliant endeavours, are doing much to clarify the issues and have, particularly by synthesis of hormones, made it possible for dermatologists to attempt the assessment of their place in treatment.

GENERAL CONSIDERATIONS

Certain facts concerning the relationship between the sex hormones and the skin are well known. Acne vulgaris commonly, almost physiologically, arises at the time of puberty and persists for varying periods up to, perhaps, the age of thirty. It is more common in males than in females. Eunuchs do not suffer from acne, although it can be produced in them by injections of male hormone (Hamilton, 1941). Exacerbations of acne in women are not uncommon at the time of menstruation when the oestrogen level falls. It may be noted here that acne vulgaris in women, or exacerbations of it, is not necessarily accompanied by any menstrual disorder. Virilism in children may be associated with marked acne.

Some skin conditions manifest themselves only in pregnancy, others regularly improve or disappear in each pregnancy; some occur only at the climacteric, in the male and in the female. Finally, certain characteristic changes occur in the skin of old age or premature old age. These changes

(2) *Monilial paronychia*.

This is an extremely chronic condition. Part or whole of one nail after another is involved over a period of years. Infection is often spread by the orange stick used in manicuring the nails, damage being done to the cuticle which protects the nail fold. The nail fold is red, shiny, swollen and bolster-like, but only slightly tender. A deep fissure separates it from the underlying nail bed, from which a drop of pus may sometimes be squeezed. The corresponding part of the nail is brownish, ridged and deformed, due to nutritional disturbances of the nail bed. Infection starts at one corner of the nail fold and gradually extends along to the other corner.

Diagnosis.—The condition often involves several nails and is less acute than pyococcal paronychia. Syphilitic and tuberculous paronychia must be borne in mind. Culture is the best method of confirming the diagnosis. A pus smear or skin scraping may be examined in caustic potash or, better, after staining with Gram's iodine. The spores are gram-positive. Mycelium is scanty and septate; groups of spores congregate at the articulations.

Treatment: Digital lesions.—Most effective are applications of gentian violet in 1 per cent. aqueous solution or in a zinc cream. The affected areas should be kept dry and covered. Mercurial and fatty acid preparations are also useful. Attention to the general health may be required. Improvement is usually rapid but recurrences are common, unless the hands are kept dry. Foci of infection may persist in the mouth, bowel, nail folds, and genitalia.

Paronychia.—Treatment is unsatisfactory as few women are willing or able to keep their fingers dry for long periods. Pure phenol or a spirit lotion, e.g.:—

Liquid phenol.....	20 minims (1.2 c.cm.)
Weak tincture of iodine.....	20 minims (1.2 c.cm.)
S.V.M.I.....to	1 oz. (28.4 c.cm.)

is applied daily with a match stick, cut into chisel shape, beneath the nail fold. Care must be taken to reach the depths of the fold and not to damage the cuticle further. With care and patience, healing results in most cases after some months' treatment.

Unfiltered X-rays, 100r to the nail folds, three doses at fourteen-day intervals, are often helpful.

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but less toxic than stilbæstrol. Headache, vomiting, anorexia, lassitude and diarrhœa are among the lesser toxic effects of these drugs. The relative potency of hexæstrol and diencæstrol is still a matter of debate. These may also be given by mouth, a method which has obvious advantages when treatment may need to be prolonged. Dogmatism on the question of dosage is impossible; individuals vary much in their response and the dose must be varied from patient to patient and from time to time in the same patient. In the case of stilbæstrol, 0.5 mgm. to 1 mgm., of hexæstrol, 3 mgm., and of diencæstrol, 5 mgm., is a reasonable initial daily dose for women, given during the period and for fourteen days after it. In some cases, for reasons not fully understood, perhaps because of failure to absorb, perhaps because they are destroyed in the liver, oral administration of æstrogens fails. Recourse must then be had to the intramuscular route or to inunction. Æstrogens in a suitable base are well absorbed from the skin, producing both a local and general effect. Dosage, of course, is a little difficult to control by this route. Subcutaneous implantation of pellets should only be employed by the very expert. Absorption by any route can be judged by certain physical changes; in the female slight enlargement of the breasts, pigmentation of the areola, increase in size, secretion, often visible from the apocrine glands around the nipple, and a feeling of lassitude. Changes of menstrual function are virtually the rule; these changes may amount to no more than an irregularity but increased menstrual loss is not infrequent, the result of an artificial metropathia hæmorrhagica. Severe flooding as a result of treatment may occur and is an embarrassment to both doctor and patient. Equally, renewal of uterine bleeding in a post-menopausal patient is an unpopular surprise. The ideal patient, of course, is the one who has had a hysterectomy. It is possible that a technique combining the use of corpus luteum hormone will be devised to control this bleeding.

In males, similar breast changes may occur in association with the same feeling of lassitude, poor growth of hair on the beard area, weakening or loss of libido, impotence and even in some cases shrinking of the external genitalia. Sterility quite certainly occurs during treatment; how far this is temporary or persists after treatment is not clear and the answer to this vital question is not easy to discover. The risk, however, of permanent sterility is so grave that it is doubtful whether the use of æstrogens in males is ever justifiable. Certainly their use must be restricted in the present state of knowledge to the treatment only of severe and otherwise hopeless cases. The danger must be explained to the patient, and it is wise to have his signature that he is aware of the risks. If these drugs are given to males the dosage to produce any effect must often be high; as much as 15 mgm. of hexæstrol a day may be required.

The preparations of male hormone in common clinical use are *testosterone propionate* and *methyl testosterone*. The propionate has only slight activity when given by mouth and is therefore usually given by intramuscular injection, in doses of 5 to 25 mgm. about three times a week. *Methyl testos-*

occur, not because of a simple deficiency of one hormone or of excess of another, but because there is a lack of balance between them. This may perhaps be clarified by saying, with apologies, that there is no such thing as a pure woman any more than there is a pure man. The bisexuality of all of us, although the degree of bisexuality varies, is important to remember when the effect of the sex hormones on the skin is considered. Furthermore, the "new look" cannot disguise the increasing masculinization of the female. The ideal woman of nature is devoted to her home, her husband, and her children and almost cow-like in her submissiveness and placidity; with this disposition goes the perfect schoolgirl complexion. The relative increase of androgen that appears to circulate in the blood of the woman of to-day may be responsible for the increase in her aggressiveness and desire for a wider participation in affairs. The reverse, of course, may be true, i.e., that increasing freedom has led to the increase in androgen. Similarly, it is at the time of the menopause, when there is a relative increase of androgen, that women so often start to manage not only their own homes and husbands but the local W.V.S., or whatever it may be. This psychological evidence of bisexuality and of the relative increase of androgen is mirrored by the changes in the skin. The whole question has been admirably discussed by Cawadias (1946).

A further point must be stressed—the varying sensitivity of tissues to endocrines. Bourne (1947) has recently emphasized this concept of the tissue receptor mechanism as put forward by Bloch (1931) in his discussion of the cause of acne vulgaris. For example, severe acne of the face is by no means always accompanied by acne of the back; seborrhœa of the body may be intense and yet the scalp is flourishing and scurfless.

No account of the sex hormones and their part in the so-called *seborrhœic* eruptions is complete without reference to Darier's (1928, 1936) conception of *la kéruse*, which he considered to be the soil on which these eruptions flourished. Barber (1929) has elaborated this point of view and further (1948) shown that the factor responsible for *la kéruse* is stimulation of the epidermis, the hair follicles and the sebaceous glands by androgens, resulting in thickening of the skin and patulous pilo-sebaceous orifices, particularly on the scalp, the centre of the face, forehead and temples, chin, the nape of the neck, the presternal and interscapular areas. Infective, dietetic and other factors in the development of the seborrhœic state can play their part only in the presence of, or as a result of, the effects of relative excess of androgens.

PREPARATIONS

The synthetic preparations have to all intents completely replaced the products obtained from natural sources.

Stilbæstrol, experimentally and clinically, appears to fulfil the functions of the natural products, may be given by mouth and is relatively cheap. *Hexæstrol* and *dienæstrol* are other synthetic œstrogens slightly less potent

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terone, although active by mouth, is best given in the form of "linguets" placed under the tongue and allowed to dissolve slowly; 5 mgm. three times a day is a reasonable initial dose in dermatological conditions. A maintenance dose must be determined by the method of trial and error. By this route in an average intelligent patient absorption is assured with no possibility of the destruction of the drug in the intestine or by the liver. Inunction, using these preparations or testosterone itself, has been successfully employed in dermatology, but since the effect required is usually a general and not a local one the oral or sublingual route is more acceptable to the patient and is more easily controlled. Subcutaneous implants are the ideal if treatment has been shown to be effective and must be prolonged.

There is no clear-cut indication for the use of androgens in skin conditions in women. Prolonged administration in women may cause growth of hair on the lip and beard area, enlargement of the clitoris, and other signs of masculinization.

There is a danger in both sexes that subsequent to the prolonged use of these hormones there may be a relative failure spontaneously to produce them in the body. It has also been suggested that the pituitary gland may not resume its full functions. On the other hand, with the doses commonly used there is no danger of any carcinogenic effect. It must therefore be stressed that the administration of the sex hormones is not without danger, and they must on no account be given unless the indication for their use is clear in the mind of the practitioner and he is well aware both of what he is trying to achieve and the possible dangers.

It will be seen from this preamble that in dermatology oestrogens may be of value in the treatment of the seborrhoeic eruptions in women, rarely in men, and of certain conditions arising at or about the menopause. The indications for androgen therapy are confined almost entirely to the senile changes of the skin of the male. These various conditions will be briefly discussed.

ACNE

Acne vulgaris.—Whatever may be its cause or causes, and the literature is vast and contradictory, and at whatever time of life it occurs, the essential fact is that androgens predispose to acne and oestrogens inhibit it. The comedo, the hall mark of acne, develops because of hyperkeratosis at the mouth of the follicle. Thus, the patulous sebaceous follicles, and the muddied complexion which so often goes with acne as a result of increased keratinization, are all due to androgen stimulation. The severity and the pleomorphism of the condition depend upon individual susceptibility, on tissue susceptibility, and on secondary factors, such as diet and infection. It is against these secondary factors that treatment must first be directed, and only when these measures fail should administration of oestrogens be considered. It is probably wise never to use them at all in women under the age of twenty. The habit of giving a small routine dose to all patients of either sex with acne can be mentioned only to condemn it.

Acne conglobata.—This is a form of acne in which large plaques develop and break down to form oily abscesses and burrowing sinuses. It is a condition so severe, so debilitating and so chronic, that it is perhaps the one disease in which œstrogens in large doses are justifiable in males.

Acne rosacea.—The etiology of acne rosacea is not clear; there is evidence to suggest, among others, an endocrine factor. This may be a straightforward relative increase of androgen or, it has been recently suggested but not substantiated, the development of hypersensitivity to androgen. If the history suggests an endocrine factor and other lines of treatment have failed œstrogens will in some cases effect a cure.

SEBORRHŒIC ERUPTIONS

It seems probable that these eruptions are the result of infection by certain organisms, notably the pityrosporon of Malassez, which by its action permits invasion by other bacteria, the *Micrococcus cutis communis* (the morococcus of Unna), the staphylococcus, and the streptococcus. It is again œstrogen-androgen imbalance which produces those changes in the skin which allow these organisms to flourish. Dietetic errors, metabolic disorder, and psychological disturbance cannot be discounted as subsidiary and often important factors. It is against these that treatment must first be directed, and only if success is still elusive should œstrogens be tried. In males they must be reserved for the otherwise heartbreaking case.

PITYRIASIS CAPITIS

This and the next stage in its development, pityriasis steatoides, are of course usually an integral part in the story of both acne vulgaris and the seborrhœic eruptions. Sometimes it occurs of itself; measures directed at care of the scalp and the infective factors should suffice without recourse to œstrogens. It is associated sometimes in menopausal women with a male type of alopecia, the hair receding at the temples and a bald patch appearing at the vertex. Local inunction of a 2½ or 5 per cent. œstrogen ointment is usually very satisfactorily successful unless atrophy of the hair follicles has already proceeded too far. Hair follicles in the scalp are exceptional in that they are stimulated by œstrogens and inhibited by androgens.

MENOPAUSAL CONDITIONS

Verruæ seniles.—It must be realized that any of the diseases so far discussed may also appear, sometimes for the first time, at the menopause. Verruæ seniles, sometimes called seborrhœic warts, are the flat-topped, circumscribed, greyish or brownish papules or little tumours with adherent, slightly oily scales which appear on the trunk, rarely elsewhere, of the middle aged or older. Œstrogens in women and androgens in men will cause all but the very large lesions to involute. This is sometimes necessary for cosmetic reasons or if the warts cause troublesome itching.

Keratoderma climactericum.—Haxthausen (1934) used this term to describe a condition of hyperkeratosis arising at the time of the menopause and mainly involving the pressure points on the soles and the palms. It is eminently treatable by œstrogens, and the results of such treatment are excellent.

Other menopausal conditions.—A number of conditions may first manifest themselves at the menopause and it is tempting to assume some relationship. Among these are urticaria, Fox-Fordyce disease, pruritus vulvæ and kraurosis vulvæ and, perhaps, psoriasis. This is dangerous ground and it must be stressed that there are many other causes for these conditions. Only after searching investigation has failed to reveal one of these other causes can œstrogen deficit be blamed. In the two vulval conditions local application of an œstrogen ointment is often more successful than treatment by mouth or by injection. Finally, senile pruritus in women can in some cases be relieved by administration of œstrogens.

SENILE MALE SKINS

The therapeutic use of androgens in dermatological conditions is all but confined to the treatment of senile changes in the skin. They can produce striking improvement in old gentlemen with itching, degenerative skins. The state of the pubic hairs is a valuable guide to treatment. If these are curly, male hormone will do no good. If, however, they are straight and lifeless, androgens will restore them, the skin and to a certain extent their owners. The skin will after a month or two recover some of the suppleness and texture of youth, if not quite that of the proverbial part of the baby's anatomy. Itching has become an ingrained habit and will persist after the reversal of the objective signs; perseverance with treatment will ultimately stop the itching and produce a sensation of general well-being. The patient who is relieved by androgen by mouth or under the tongue is an ideal candidate for subcutaneous implants.

This short review of a fascinating and, to me at least, a very difficult subject cannot be ended without a tribute to the work in this field of Dr. H. W. Barber, who has given so much thought and done so much to clarify the issues and unravel the tangles. Anyone interested more deeply in the subject is warmly recommended to read a recent essay by Dr. Barber (1948), in which the whole matter is logically and illuminatingly expounded.

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COSMETICS AND THE CARE OF THE SKIN

By GEOFFREY HODGSON, M.B.E., D.M.

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THE use of cosmetics is centuries old. Egyptian tombs provide evidence of lead eye and face paints (kohl) which the departed took with them on their last journey as cosmetic aids. Nero's wife, Poppæa, is said to have bathed in asses' milk, taking with her a herd whilst on her travels. To-day there is no need for such a complicated supply system, as modern mass production backed by the force of advertising has made cosmetics an integral part of everyday life. The advertising claims regarding the health of the skin may be such as to make the average medical man wonder how far such claims can be justified; likewise may he wonder how often the innocent buyer of such preparations may pay the price of her vanity by developing an "occupational dermatitis" in her work of beautification. It must be stated at once that dermatitis from cosmetics is a rare occurrence. It is only necessary to try and estimate roughly the enormous cosmetic consumption of the community as a whole, and to think of the isolated cases of skin trouble from this source, to put the matter in its proper perspective.

HAIR PREPARATIONS

Skin irritation may result from *bleaching or dyeing*, and from hair dressing, e.g. permanent waving. Dyeing may cause the hair to become brittle and break off short; Ovid mentioned this. To bleach the hair "platinum blondes" use hydrogen peroxide and ammonia, and the same ill-effects may ensue. Experienced hairdressers will advise against it if the hair is not suitable for bleaching; amateur efforts produce most cases. Hair dyes are vegetable and mineral in origin or of the para group which causes most trouble. Vegetable dyes or tints, such as walnut and henna, e.g. henna washes, are generally quite safe; synthetic henna tints may act like the para group. Mineral dyes, e.g. silver nitrate, are seldom used, as the texture of the hair may be coarsened thereby; they act by deposition of a layer on the hair shaft. The third group includes paraphenylenediamine and pyrogallol; Ingram (1947) has suggested, after patch testing 1000 persons, that 4 per cent. of the population are sensitive. This sensitivity may be present initially or develop as a result of several applications of the dye. The danger is contact dermatitis. In some cities in America the health authorities insist on a patch test being carried out on the neck line for twenty-four hours before the first occasion on which the hair is dyed. A recommendation that the dye should be first tested in such a way should be stated on the label of the bottle.

Dermatitis from hair dyes is suspected by the history and by the appear-

ance of redness, with itching on the eyelids, forehead, behind the ears, and on the back of the neck. If a sudden weeping of the whole scalp be caused, then the condition may be mistaken for an acute seborrhœic process. Spread of the eruption may occur to the elbow flexures. Conjunctivitis and inflammation of the cornea may be produced. A patch test can be employed in confirmation of the diagnosis. "First-aid" treatment requires immediate washing with soap and water to remove the excess dye. Next, a solution of hydrogen peroxide is applied to oxidize the dye to a non-irritant compound; then the hair is washed again with soap and water. The dermatitis is then treated on routine lines with turban compresses of potassium permanganate, 1 in 5000, or normal saline.

Dermatitis from hair tonics is fairly common, and on the same areas as from the other preparations. Dermatitis of the hands may occur. Spirit in lotions may produce scaling of the palm of the hand into which the tonic is poured before its application, and cracking of the finger tips from rubbing it into the scalp. Brilliantines and "hair" creams can produce a folliculitis or acne-like condition with comedones on the forehead. Men, women, and young boys may be affected. Perfume in such preparations can lead to pigmentation of the forehead along the hair margin.

In permanent waving the keratin of the hair sheath is softened by an alkali, the hair wound round curlers and steamed. Some redness of the skin and discoloration may occur along the forehead; this may be due to the alkali or the heat of the steaming. Grey, bleached, or dyed hair may break off short after such a process. Thermal burns of the neck may occur. The new cold-wave technique employs thioglycollic acid to soften the keratin hair sheath; dermatitis, damage to the liver by absorption, and brittleness with breaking off of the hair may be untoward events.

Hair lacquers are employed to keep the hair wave in position; sensitivity occurs after some days' delay. Signs of dermatitis appear on the back of the neck, eyelids, or face. Asymmetrical patches occur on the arms in contact with the head at night. The husband and the baby may both develop patches of dermatitis on the face.

NAIL PREPARATIONS

Manicuring may itself cause traumatic damage to the nail fold. I have seen a patient who developed an acute *B. coli* paronychia of nearly all the fingers following an unskilled self manicure. She attributed the inflammation to the use of a new type of varnish, but this was not so; dermatitis from nail preparations shows itself as a rule on the face and not on the fingers. Liquid nail polishes and lacquers cause dermatitis as a result of plasticizers (for flexibility), perfumes, and commonly from dyes (eosin, maroon, rhodamine B) which also cause photosensitization, and will react on exposure to sunlight.

Dermatitis is not at all uncommon and will show as small, dry, itchy patches with redness and scaling of the eyelids, chin, cheeks, ears, clavicles, and on the side of the neck; occasionally on the nape of the neck as a patch of thickened skin. Much more commonly, however, a patch of this type is a lichen simplex chronicus (neurodermatitis), or a localized area of seborrhœic dermatitis. These may be menopausal in onset. Fingering of the area by the patient during the interview may give a clue at once. Rare sites are on the legs after a ladder in the stocking has been stopped with polish; around the anus and vulva, presenting as vague itching; and on the baby's face from the mother's nails, as examples of infantile "eczema". Nail polish in the linings of shoes may cause dermatitis of the dorsum of the feet and toes. Removal of the cause will lead to immediate improvement. A patch test may not give a positive reaction.

Cuticle removers may contain caustic potash, salicylic acid, and triethanolamine. The nail may be damaged by the caustic or the nail fold inflamed. Polish removers are largely acetone solutions. Brittleness of the nails, dryness and splitting may result, or chemical paronychia.

It might be argued that nail preparations have some influence in the care of the skin. The acetone remover may contain tincture of benzoin or cellulose acetate. Presumably such a combination must have some antiseptic effect that may help to sterilize the area. Routine nail attention and the use of such preparations may avoid the paronychial infections to which poorly manicured nails may be subject, and may conceivably protect against the troublesome nail infections so common in housewives and those engaged in occupations in which the hands are continually in water.

FACE AND BEAUTY CREAMS

These creams are variations of the oil-in-water and water-in-oil emulsions. They are advertised as cold, vanishing, foundation, cleansing, lubricating, and gland creams, skin and tissue foods. A *foundation cream* serves as a base on to which the powder is applied; cleansing creams remove the previous make-up. Some women once employed at least three or four different creams, but "all purpose" creams are now available. The introduction of new emulsifying agents and of the lanoline derivatives have superseded the older greasy cold creams, e.g. rose water ointment.

Vanishing creams consist of stearic acid, grease as cocoa butter, liquid paraffin or glycerin, water or alcohol, with an emulsifying agent (borax, triethanolamine). These creams form a non-greasy surface on to which powder will adhere; they are so constituted that no excess of grease is perceptible on the skin after application, hence they seem to "vanish". *Cleansing creams* are similar but have the melting point of the fats below that of the skin, so that they become liquid on being applied. To these creams may sometimes be added a cleansing agent, such as sulphonated

ance of redness, with itching on the eyelids, forehead, behind the ears, and on the back of the neck. If a sudden weeping of the whole scalp be caused, then the condition may be mistaken for an acute seborrhœic process. Spread of the eruption may occur to the elbow flexures. Conjunctivitis and inflammation of the cornea may be produced. A patch test can be employed in confirmation of the diagnosis. "First-aid" treatment requires immediate washing with soap and water to remove the excess dye. Next, a solution of hydrogen peroxide is applied to oxidize the dye to a non-irritant compound; then the hair is washed again with soap and water. The dermatitis is then treated on routine lines with turban compresses of potassium permanganate, 1 in 5000, or normal saline.

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greasy cream for face cleaning. The use of suitable creams in fair-haired, sensitive-skinned babies might prevent that type of infantile "eczema" which not uncommonly starts in the early months of extra-uterine life as a sequel to soap, contact with wool, and winter chapping.

Other dermatological indications are in the "irritable faces" of women at the menopause—rosacea subjects without excessive sebaceous activity who ill tolerate soap—and in skin cases convalescent from acute facial dermatitis of whatever origin, in which the skin is dry, irritable, and has not had time properly to "harden up". Sun-sensitive individuals and lupus erythematosus cases can be protected against sunlight by the use of sun-screening face creams. These contain phenyl salicylate 10 per cent., quinine sulphate 2 per cent., or esculin 2 to 4 per cent. as a chemical preventative, or zinc oxide as a purely mechanical barrier.

Soap is indicated in puberty or adolescent acne, but is sometimes not well tolerated by many adult acne faces. Here a face cream of oil-in-water emulsion type can be employed therapeutically as a degreasing cleansing agent and cosmetically as a foundation for the face powder. Nail creams are helpful as an emollient application for use in brittle nails, by virtue of the lanoline, wax, and triethanolamine, which they contain.

Little, however, can be said in medical support of those creams containing vitamins and the sex hormones as "skin foods". "Gland" creams are also in vogue for increasing bust development and in the treatment of superfluous hair. It is unlikely that vitamins are included in sufficient concentration to have any effect at all, but they are presumably harmless. In the case of vitamin D₂ (calciferol), however, toxic results could ensue from absorption if the vitamin was used in sufficient amounts. There is no evidence that oestrogens are locally carcinogenic when applied to the skin, but there is no question that oestrogens are absorbed by the skin. Barber (1948) has seen cases of uterine bleeding and swelling in the breasts following inunction of 5 per cent. and 2 per cent. dienoestrol cream to quite small areas of skin. The risk of carcinoma developing in the uterus and breasts as a result of the prolonged local skin application of oestrogens is probably only a very doubtful possibility. However, a theoretical risk alone should be sufficient argument against their use until the matter is beyond dispute. The indiscriminate use of oestrogens in cosmetic creams can only be strongly disapproved of by medical men at present.

PERFUMES, POWDERS, LIPSTICKS, EYE PREPARATIONS, DEODORANTS

Perfumes may produce dermatitis or pigmentation of the skin, but uncommonly. Perfumes are often included in other types of cosmetics and may be the active constituent causing skin irritation. Dermatitis may show itself as redness and scaling on the eyelids or behind the ears. Application

castor oil or coconut oil. Cholesterin and lechithin are commonly added as the emulsifying agent. *Skin "foods"*, in addition, may contain oils of almonds, raisins, turtle, avocado pear, and grape seed, which are all readily absorbed. The lanoline extracts, cholesterol and oxycholesterol, are mainly employed as they produce a neutral water-in-oil cream and a smooth, pleasant product. The sex hormones, as well as vitamins, may be added.

Creams seldom cause irritation of the skin. Occasional cases are attributable to emulsifiers, lanoline, preservatives, or the perfume content, which may cause dermatitis or pigmentation. A dermatitis would appear over the area covered by the cream. The appearance may be like a mask, as the hair margins, sides of the neck, and under the chin may appear white by contrast with the redness and scaling elsewhere, having escaped contact with the preparation. Most *freckle creams* contain peroxides, although some employ mercurials; individuals are often sensitive to mercury and react by dermatitis. Groekerman (1925) described a slate-grey pigmentation of the skin due to such a preparation. The effect of freckle removers is only temporary if the action on the skin is severe the melanoblasts may be stimulated causing the appearance of darker freckles when they re-form. *Greasy creams* may irritate some people, and a folliculitis may present. Soft paraffin and liquid paraffin are capable of producing blackheads and acne-like pimples especially in a greasy skin.

It is most unlikely that the routine application of modern face creams can have any ill-effects on the skin; they certainly do not increase the growth of hair. MacKenna, in 1930, suggested that rosacea cases might be worsened as a result of blockage of the sebaceous and sweat glands if vanishing creams were applied without proper cleansing. A greasy skin might ill tolerate the routine use of a greasy cream if it were not removed by soap and water, but the constituents of modern creams are well absorbed (Harry, 1946), and the creams can be suited easily to the type of skin in question by alteration of the oil-water emulsion bases to get the required emollient or degreasing effect. Hence in greasy skins prolonged use of modern creams probably does no harm at all. As, however, getting the right cream is a matter of trial and error for the average woman buying cosmetics over the counter, a subject with a greasy skin would be wise to supplement her skin cleaning with soap and water.

Cold creams and the modern creams with cholesterol, oxycholesterol, and lechithin (a normal skin constituent) have a definite place in the routine care of the skin. Although they cannot influence the ageing processes that lead to senile atrophy and "crows' feet", their continued emollient action can only be for the good, especially in dry or ageing skins. They supersede the use of oils in vogue in ancient times for preserving the skin. Creams of this type can be used for cleaning naturally dry skins or those that dislike soap; they protect the skin against cold and winds. Ichthyotic individuals or those dry-skinned persons with atopic eczema can use with advantage a

eosin group of dyes may photosensitize; some indeed are only irritant on exposure to sunlight. Dermatitis with redness, weeping and crusting along the lips is obviously due to a lipstick or lip salve. In general it can be said that the routine use of lipstick can help to counteract winter chapping or cracking of lips in susceptible persons. Some manufacturers include sulphonamides in lipsticks for chapped lips. It may irritate or sensitize to sunlight, and from the dermatologist's viewpoint should be condemned.

DIAGNOSIS

Cosmetic dermatitis is not common. Plastic or chromium nickel spectacle frames, hats, necklaces, plastic dress ornaments, tooth pastes and powders, fruits, and mouthwashes may produce an irritation of the area in question which may closely simulate cosmetic dermatitis.

Nail polish and perfumes are more implicated than other preparations, and cosmetics such as powders and creams may irritate only as a result of their perfume content. Asymmetrical dry, red, itchy scaling or pigmented areas on the face and neck, especially if associated with occasional swelling of the eyelids, are often indicative of these types of cosmetics.

The history is all-important and should be inquisitorial. The use of a cosmetic may be so routine that patients genuinely forget that they have used it. In cases of doubt the patient should forego the use of all cosmetics for at least four to six weeks. It is usually permissible on such occasions to allow lipstick and a non-perfumed talc powder as a concession to vanity. The dermatitis will occur on the areas to which the cosmetics have been applied, except in the case of nail preparations, which commonly show on the face, eyelids, or neck. It will improve when the application is stopped, and this is a better diagnostic pointer than a patch test, which may often give a negative reaction. When photosensitive dyes are suspected the patch test should be exposed to sunlight for one to two hours.

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by a spray or in a face cream shows itself diffusely on the face or neck. Perfume used by others may irritate. An unusual case has been under my care.

A lady of forty-six for two years had had brownish-red, dry scaling patches on the face, and sudden attacks of acute swelling of the eyelids. Visits to the cinema provoked such attacks and perfume was suspected, although the patient used none herself. The diagnosis became clear when her sister came to the front door one day and, though she did not enter the house, an acute attack followed within half an hour. Since her sister has given up the perfume no further attacks have occurred. A patch test was positive.

Pigmentation occurs in streaks or patches on the face, neck, and behind the ears. The term "berlocque" was used by Rosenthal to describe the pendant and necklace-like distribution. Oil of bergamot is said to be most commonly at fault, and Freund, in 1916, first described this uncommon localized facial pigmentation after application of Eau de Cologne and sunbathing. It has been suggested that the essential oils of the perfume are dissolved by perspiration, producing photosensitizing substances. Photosensitization by perfumes in face powders and creams may produce a bronzing effect of the whole face as if the skin was sunburnt.

A typical *face powder* contains calcium or magnesium carbonate, talc or kaolin, magnesium or zinc stearate, titanium or zinc oxide, with colouring matter, and sometimes perfume. The stearates are used for adhesion of the powder, talc for slip, whilst titanium dioxide gives a good coverage. Face powder has some sun protective effect, especially if the zinc oxide content is high.

Rouges are on the whole harmless. *Mascara* is also innocuous; it is usually lampblack in paraffin and petrolatum. Cleopatra is said to have darkened her eyebrows and lashes with a substance of this type. Eyebrow pencils are finely powdered carbon in a waxy base. Itching of the eyelids and swelling, with blepharitis and styes, can occur from eyelash dyes.

Deodorants are marketed as liquids, creams, or powders. They inhibit perspiration through an astringent action or they simply disguise the odour. Of the former, aluminium salts being most effective are most used; susceptible skins are irritated. Hexamethalene tetramine decomposes with sweat through formaldehyde to formic acid. Formaldehyde may irritate. Zinc peroxide, hexamine, and perfumes are solely for deodorizing. Irritation signs are redness, vesicles, weeping or folliculitis localized to the axillæ. In dye dermatitis from dresses or dress shields the apex of the axilla is clear. In seborrhœic dermatitis of the axillæ, evidence of a similar condition will probably be found elsewhere. Well-established proprietary deodorants may safely be prescribed medically for axillary hyperhidrosis and have a place in treatment. Rotting of fabrics will occur if the clothes are put on before the application has dried.

Lipsticks contain colouring in a solid oil-beeswax-cocoa-butter stick base. Skin irritation is seldom caused, but the indelible types containing the

eosin group of dyes may photosensitize; some indeed are only irritant on exposure to sunlight. Dermatitis with redness, weeping and crusting along the lips is obviously due to a lipstick or lip salve. In general it can be said that the routine use of lipstick can help to counteract winter chapping or -cracking of lips in susceptible persons. Some manufacturers include sulphonamides in lipsticks for chapped lips. It may irritate or sensitize to sunlight, and from the dermatologist's viewpoint should be condemned.

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PRESENT INDICATIONS FOR SULPHONAMIDES IN VENEREAL DISEASES

By R. R. WILLCOX, M.B., B.S., M.R.C.S.

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THE general introduction of the sulphonamides in 1937 was the first of a series of breath-taking events in the revolution of the treatment of venereal diseases since Ehrlich discovered salvarsan over a quarter of a century before. The most striking and valuable results were manifest in the treatment of gonorrhœa, which was rendered a disease of reasonable hazards instead of the protracted and often crippling complaint that formerly pertained.

Thus in contrasting the effects of the sulphonamides with the previous treatment in the same clinic, Cokkinis and McElligott (1938) reported 250 male and 139 female patients with acute gonorrhœa who received only local irrigations and vaccine. An apparent cure was obtained after one month in only 9.8 per cent. of males, and the average period for apparent cure was 101 days, with no less than 18.1 per cent. remaining uncured at six months. A further 19.6 per cent. of males relapsed after apparent cure, and as many as 90 patients (36 per cent.) developed complications. The results in females were no less discouraging. The average time before abolition of the gonococci was achieved in the smears and cultures was 3.2 and 2.7 months for the urethra and cervix, respectively, but an average of 5.5 months elapsed before no local evidence of disease could be found, and 35 cases (25.2 per cent.) developed some complication.

Even employing the weaker sulphonamides such as sulphanilamide the initial results were dramatic for, with a single course of treatment, an apparent cure was obtained in a matter of days in 60-80 per cent. of cases, whilst the incidence of complications was slashed to below 10 per cent. The introduction of sulphapyridine, although increasing to some extent the toxic effects both major and minor, also improved the effectiveness, which now approximated 80-90 per cent. of cures. The later use of sulphathiazole and sulphadiazine maintained or improved upon the clinical results, removing nearly all of the minor toxic effects and reducing some of the more serious.

The first major *toxic complications* to be feared were those of leucopenia, agranulocytosis and hæmolytic anæmias, although these proved to be no large-scale menace. More important were the renal disturbances due to the formation of the less soluble acetylated products in the urine, with the production of hæmaturia and oliguria which, if untreated, could in turn lead to anuria and death. By keeping the daily dose in the region of 4 to 6 gm., and by ensuring that an adequate amount of fluid was being taken (a maximum of six pints daily being recommended by the Medical Research Council (1945), and more by many clinicians), the renal complications were kept at a minimum. If the total dose employed was under 30 gm., and the

period of administration less than a week, the blood dyscrasias rarely caused trouble. The danger of urinary acetylation has since been shown by Lehr (1947) to be even further reduced if three sulphonamides, e.g. sulphadiazine, sulphathiazole and sulphapyridine as "sulphatriad", are combined, for crystallization occurs in proportion to the amounts of the individual members and not according to the total quantity of sulphonamides present.

Repeated internal use of the drugs for all sorts of minor conditions, and their widespread adoption for local creams and ointments, led, however, to a large number of persons becoming sulphonamide sensitive, and various skin eruptions, from the erythematous and morbilliform to an obvious weeping dermatitis, were increasingly reported (Park, 1943). Even the use of sulphanilamide powder for prolonged periods to a minute area such as that of a cauterized penile wart could produce a generalized dermatitis (Willcox, 1943). Although the sensitization dermatoses could be prevented by refraining from the use of the drugs for trivial complaints, these conditions, although not serious to life, continued to be a nuisance.

Resistant strains.—From the beginning there were always some cases of gonorrhœa (5 to 15 per cent.) which were continually resistant to sulphonamides. A few of these could be made to respond to a second course of another member of the sulphonamide group, and a greater number, if the second course was combined with fever, in the form of intravenous T.A.B. vaccine or hyperthermy. As time went on these cases became increasingly more troublesome and, as resistant strains which maintained their resistance through many generations *in vitro* were easily produced, so it appeared that drug-fast strains were being propagated in man. Indeed most venereologists can remember seeing at least one series in which several men contracted a resistant gonorrhœa from the same woman.

Although the success rate at home had somewhat declined by 1943, it was overseas that the greatest difficulties were being experienced, especially in those areas where military occupation coincided with the widespread use of sulphonamides by the civilian populations. Thus in Italy, Campbell (1944) encountered success rates of only 20 to 25 per cent. In West Africa, where these drugs had previously been in such short supply as to allow only miserably ineffective doses to be given for gonorrhœa, a general success of 80 to 90 per cent. was at once obtained when adequate doses of sulphathiazole were given (Willcox, 1946), but, as the local population became saturated, the numbers of resistant cases mounted. This doleful state of affairs was only partially relieved by the ever increasing use of fever therapy and the introduction of penicillin was welcomed with both hands, for those cases which formerly were resistant responded like magic to the new drug. The profession anxiously waits lest the events described occur again with penicillin. At present fast strains of gonococci have been cultivated *in vitro* (Bahn, *et al.*, 1945), but so far there has been no evidence of clinical resistance either here or in the United States (Parkhurst, *et al.*, 1947).

GONORRHOEA

The epoch-making discovery by Mahoney and his associates (1943) that penicillin would also cure syphilis has saved a remnant of the treatment of gonorrhœa to-day for the sulphonamide group of drugs. The dose of penicillin required to cure gonorrhœa (200,000 to 300,000 units) is only a fraction of the 3 to 6 million units used in the treatment of syphilis, and the duration of the treatment for gonorrhœa has been reduced to a single injection, whereas that of syphilis is at least seven to fifteen days. This means that penicillin, given for gonorrhœa to a patient who is incubating syphilis from the same or previous exposure, may have the result of being subcurative or suppressive for syphilis, with the subsequent development of the disease when the patient is no longer under medical care.

With sulphonamide-treated cases of gonorrhœa the period of follow-up and repeated clinical and serological examinations, to ensure that the patient is not also developing syphilis, is three months. As it appears that penicillin may prolong the incubation period of syphilis, the period of such surveillance in penicillin treated cases is placed at six months in this country and by Moore (1946) in the United States at four months. Critical examination of the published cases leads to the supposition that syphilis arising after small doses of penicillin for gonorrhœa is seldom evident for the first time after three months (Cronin, 1947), and probably a four months' surveillance is sufficient. Nevertheless, sulphonamides are recommended in all cases of gonorrhœa in which the risk of syphilis is more than the average. This includes:—

(1) All cases of gonorrhœa with an accompanying undiagnosed genital sore. Once *T. pallidum* has been isolated, the penicillin given for the syphilis is more than sufficient for the gonorrhœa. As three negative dark-field examinations on three successive days, and repeated negative serological tests over a three months' period, have to be obtained before syphilis may be entirely excluded, it is a wise measure, if possible, to treat the gonorrhœa solely with sulphonamides.

(2) All cases with definite enlargement of the inguinal glands. This is not found in simple gonorrhœa unless there is a complicating periurethral or Bartholin's abscess, or associated balanitis or genital sore. The possibility of the syphilitic origin of the adenitis in the absence of genital sore may be sometimes decided by gland puncture.

(3) All cases showing a "false positive" serological test for syphilis should also be given sulphonamides until all possibility of syphilis has been refuted by the obtaining of two successive negative complement fixation and flocculation tests.

(4) All cases which are known to have had recent exposure with a case of infective syphilis.

(5) All cases of gonorrhœa which have relapsed or recurred following penicillin and in which there is a history of chills, fever and headaches within a few hours of its administration. (This may be evidence of a Herxheimer reaction to concealed syphilis.)

The sulphonamide drugs may also be employed in all cases of *penicillin-resistant gonorrhœa* (which are not at present occurring) and all cases of urethritis and cervicitis in adults, and vulvo-vaginitis in children, when there is either repeated relapse following penicillin or a prolonged infection

with non-specific organisms. Given orally they are also effective in subacute salpingitis following, but not apparently due to, active gonorrhœa.

The drugs of choice are either sulphadiazine or sulphathiazole: 4 to 5 gm. may be given daily to adults in divided doses for five to seven days. The actual success rates with these drugs at the present time cannot be much above 50 per cent. and failure to respond to them often causes the position of the desirability of withholding penicillin to be reviewed.

Prophylaxis of gonorrhœa: systemic.—Three doses of 2 gm. each of sulphathiazole, given at intervals in the twenty-four hours following exposure, have been shown to prevent the appearance of clinical gonorrhœa. Whilst this is of interest as a short-term policy in a venereally dangerous locality, it is not without its dangers, for frequent administration of small amounts of these drugs, besides the inherent risk of toxic effects, may induce hypersensitivity and render them dangerous at a later period when they may be more urgently required in the case of more serious illness. The other possibility is that gonorrhœa may be acquired and aborted without being radically cured, and without the usual final tests of cure the patient may be living in a state of false security.

Local.—Less dangerous, but also less easy to perform when promiscuity follows a debauch, is the instillation into the urethra after exposure of a 10 per cent. sulphathiazole cream, which would appear to be effective in lowering the incidence of the disease. Other local uses of sulphonamides in the management of gonorrhœa include the use of sulphanilamide powder as a dressing to wounds of incised or burst peri-urethral or Bartholin's abscess. The sulphacetamides (albucid), owing to their forming near neutral solutions, are suitable for conjunctival instillation of a 2.5 to 10 per cent. solution in gonococcal ophthalmia, conjunctivitis, or as a prophylactic should infected matter accidentally contaminate the eye, though penicillin solutions are even more effective.

CHANCROID

Sulphonamides are still, in this country, the drugs of choice in the treatment of soft sore. Penicillin, in addition to not being particularly effective, is contraindicated for fear of masking a protean syphilitic infection, and sulphonamides, whilst encouraging the sore to heal, do not impede the dark-field tests for *T. pallidum*.

Sulphadiazine, sulphathiazole, sulphapyridine or sulphanilamide may be given, 3 to 4 gm. daily, until a maximum of 28 to 30 gm. have been administered over a six to eight day period, unless previous healing has occurred. Of 100 consecutive cases treated in West Africa by means of different sulphonamides, the average period before the sore had healed was 12.5 days (extremes 4 to 44 days) (Willcox, 1946). Locally, sulphanilamide powder may be applied to the sores with advantage when the dark-field

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STREPTOMYCIN

Although at the present time sulphonamides have a limited but nevertheless definite scope in the treatment of venereal disease, it is evident from the literature that their tenure is insecure and that streptomycin is offering a definite challenge. Supplies in this country are not yet sufficient for large-scale tests in the venereal field, but from America a number of important observations have been made.

(1) It has some action against syphilis but much less marked than penicillin, and is unlikely to be useful in that disease (Moore, 1946).

(2) It is effective against gonorrhœa: 70 out of 72 cases were reported cured by means of a single injection of 0.2 to 0.5 gm. by Chinn, *et al.* (1947). The two failures responded to re-treatment.

(3) A dose of 4 gm. daily, for only five days, has produced dramatic results in granuloma venereum and is obviously to replace the prolonged intensive treatment previously required with the antimionals (Greenblatt, 1947).

(4) *Hæmophilus ducreyi* has been found to be very sensitive to streptomycin both *in vitro* and in experimental chancroidal infections (Mortara and Saito, 1947).

As streptomycin is also effective against *B. coli* and against pleuro-pneumonia-like organisms, suggested by some as the cause of non-specific urethritis and Reiter's disease, it is therefore apparent that, apart from a limited use in the treatment of lymphogranuloma inguinale and the local prophylaxis of gonorrhœa and soft sore, the days of sulphonamides in venereology are probably numbered.

It is to be hoped that streptomycin will soon be in sufficient supply to allow these new and exciting discoveries to be fully exploited.

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 — (1946): *Brit. J. vener. Dis.*, 22, 2, 63.

tests to exclude syphilis have been completed and also to any burst buboes for periods not exceeding one week.

Prophylaxis.—A dosage of 3 to 5 gm. daily for two days following exposure has been found, if given orally, to be an effective prophylaxis against chancroid. The same indications and objections pertain as are described under the systemic prophylaxis of gonorrhœa. The procedure may be of some value in certain tropical districts where the local risks are much higher. A 10 per cent. sulphathiazole cream applied to the parts before and after exposure is also of some value, but is usually combined with a 33 per cent. calomel cream in order that syphilis may also be prevented.

OTHER GENITAL LESIONS

Systemic sulphonamides, as for chancroid, are of value during the time that the dark-field examinations to exclude syphilis are being performed in all cases showing secondarily infected genital lesions, whether these are due to septic scabies, balano-posthitis, phimosis, infected herpes genitalis or other conditions. Tests to exclude gonorrhœa must first be made. Sulphonamides are not directly effective in granuloma inguinale, but may be used as adjuvants if secondary infection persists (Med. Res. Coun., 1945).

LYMPHOGRANULOMA VENEREUM (INGUINALE)

Sulphadiazine, sulphathiazole, sulphapyridine and sulphanilamide are all suitable, although the greater toxicity of sulphapyridine makes this the last to be chosen: 4 to 5 gm. daily should be given for five to seven days. Should a second course be desired, an interval of one to two weeks should first elapse, and then it should be combined with intravenous T.A.B. or other fever therapy. Sulphanilamide powder is a useful dressing for burst buboes for periods not exceeding one week. Of 120 consecutive cases thus treated in West Africa, all exhibiting the inguinal syndrome, the average time before they were fit for discharge from hospital was 9.1 days (extremes 4 to 32 days). There were eight relapses (Willcox, 1946).

NON-SPECIFIC URETHRITIS AND OTHER URETHRAL CONDITIONS

The sulphonamides are not as a rule so successful in the treatment of this condition as in gonorrhœa, but the results, if not dramatic, are often satisfying. Penicillin too, shows a variable action. Sulphadiazine or sulphathiazole may be employed in daily doses of 4 to 5 gm. for six to seven days. Cystitis and pyelitis due to *B. coli* are also best treated with sulphonamides, for this organism is insensitive to penicillin.

Sulphanilamide powder, for periods not exceeding one week, is a useful wound dressing following circumcision, dorsal slit, cautery of warts and other minor surgical procedures.

STREPTOMYCIN

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HIGH RESECTION OF THE INTERNAL SAPHENOUS VEIN

By R. ROWDEN FOOTE, M.R.C.S., D.R.C.O.G.
Surgeon in charge of Varicose Vein Department, Harrow Hospital.

THE operation of high resection of the internal saphenous vein is now generally accepted by surgeons as being the normal antecedent of further treatment directed towards the cure of varices associated with incompetence of the valves of the long saphenous vein. Not only is this operation required for the millions of sufferers from severe varices but it is often necessary in patients with severe varicosities before an abdominal or a pelvic operation. This procedure may serve to prevent a postoperative thrombophlebitis and a possible pulmonary embolism. The term "saphenous ligation" or, as in America, "top tie" are misnomers, since the essence of the operative procedure is in the resection of the terminal portion of the internal saphenous vein, together with a careful section and ligation of all the tributaries at the sapheno-femoral junction.

The mortality of this operation, when properly performed, is extremely low, subject to ambulatory exercises being taken immediately after its completion. The details of the recurrence rate, the various types of sclerosants and their use, and the exact indications for or against operation, do not come within the scope of this article which is aimed only to demonstrate certain points to facilitate speed in performance.

The operation as now practised varies little from that described by Homans in 1916. It is customary to read in textbooks on surgery that the technique has become so standardized that a detailed description is not necessary. The purpose of this article is to show that there are some technical points which, although they may appear minor in nature and, to many readers, almost obvious, are necessary factors in the swift and careful approach to the saphenous opening. Experience in varicose clinics reveals that recurrences and complications are all too common. Unless a careful and thorough technique is adopted the operation runs the risk of falling into quite unjustifiable disrepute.

Many surgeons regard this operation as being suitable for the outpatient department. It is often an easy and foolproof procedure but may, on the other hand, present considerable difficulty and fall into the category of a major operation. Those interested should read the excellent article entitled "Hazards of Varicose Surgery" by Atlas (1943). Sepsis, uncontrollable hæmorrhage, hæmatomas, lymphorrhœa, deep vein thrombosis and embolism, may all be associated with what has been termed an easy procedure. This operation is not for the occasional surgeon, since those

intending to perform it should have an exact anatomical knowledge of the saphenous opening and should appreciate that the saphenous vein has been shown, both in the cadaver and at operation, to have so many abnormal methods of termination that normality in this area can be said to be relatively nonexistent. The operator should always remember that his patient is a normal healthy person who might well go through life quite happily in an elastic stocking. For this reason no undue risk is justifiable in the approach to a patient whose disease is essentially of a non-lethal character.

OPERATIVE TECHNIQUE

The patient should preferably be admitted the evening before the day of the operation and be given a warm bath and a complete surgical shave. An over-night sedative is advantageous if the patient is at all nervous. The leg should be examined in the erect posture and the veins marked with skin ink. Attention may be called to blow-outs by making a circular mark around these areas. The lines of the various incisions required may be marked at the same time. Tinea of the groin and dermatitis due to a pendulous abdomen should first have been excluded and treated. On the morning of the operation the leg should be prepared with surgical spirit and, if the operation is to be performed under a local anæsthetic, the pre-medication should be given at least one hour beforehand. Two per cent. novocain is a most satisfactory anæsthetic in these cases. Adrenaline (1:1000) may be added in the proportion of four drops to the ounce of anæsthetic solution.

Immediately after operation, a supportive bandage may be used with advantage in many cases. Ambulatory exercises with the limb encased in the two-way-stretch bandage help the deep venous circulation, and compress the superficial varices, helping to approximate the intima of the varices which may have been damaged by sclerosant or roughened needle. These bandages must be removed if the patient is at rest.

The following illustrations with their captions (pp. 388-391) will serve to demonstrate my views on some of the technical points of the operation.

I am indebted to Messrs. H. K. Lewis & Co., Ltd., for permission to reproduce fig. 13-16, and to the Editor of *Surgery, Gynecology and Obstetrics* for fig. 6.

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FIG. 1

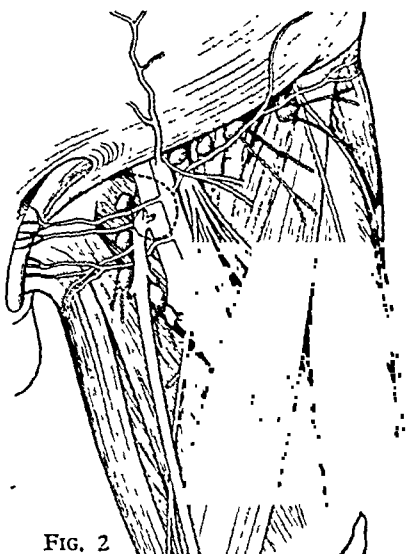


FIG. 2

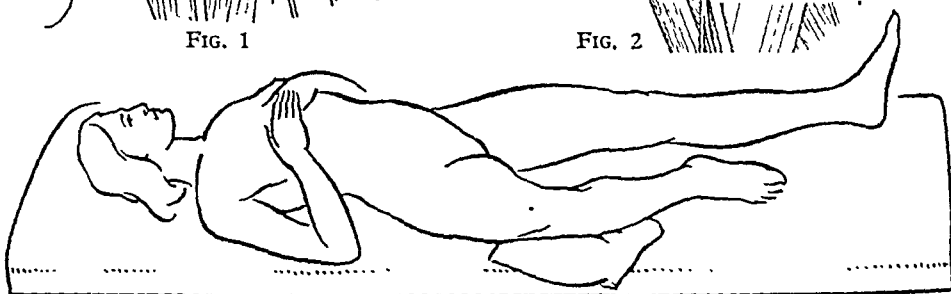


FIG. 3

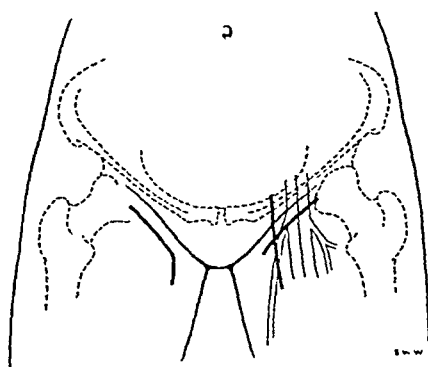


FIG. 4

FIG. 1.—The saphenous opening. Note the manner in which the deep fascia forms the ring and the common position of the superficial gland (gland of Cloqué). The angle of union of the internal saphenous vein with the common femoral vein is clearly shown.

FIG. 2.—Scarpa's triangle. The position of the saphenous opening is marked with a dotted line and the position of the femoral vein and femoral artery should be carefully noted. The position of the lymphatic glands is important and the operation may be complicated if these glands are inflamed as the result of absorption from a varicose ulcer or from tinea interdigitalis. Note the angle at which the saphenous vein joins the femoral vein. When in doubt the inward direction of the saphenous vein is an important point of differentiation from the femoral vein. When this vein is found to be varicose it is an additional point of differentiation.

FIG. 3.—A suitable position for operation. The knee is flexed and is rested on a pillow. Alternative positions are preferred by some surgeons. The legs may be widely separated on a board at the table end.

FIG. 4.—Demonstrates three of the most common forms of incision for exposing the sapheno-femoral junction. The vertical incision begins above Poupart's ligament and in fat patients should be carried higher than in the thin. It lies roughly two finger-breadths medial to the pulsation of the femoral artery. The transverse incision is best started over or just lateral to the femoral artery and carried in or just below the crease of the groin for an average distance of two inches. The "hockey-stick" incision demonstrated in the right leg is merely the transverse incision which is carried vertically at its termination and allows of a fuller exposure. Do not try to do this operation through too small an incision (Ogilvie 1946). As the patient is ambulatory, he must not be submitted to an incision the length of which might cause delayed healing owing to early movement of the limb.

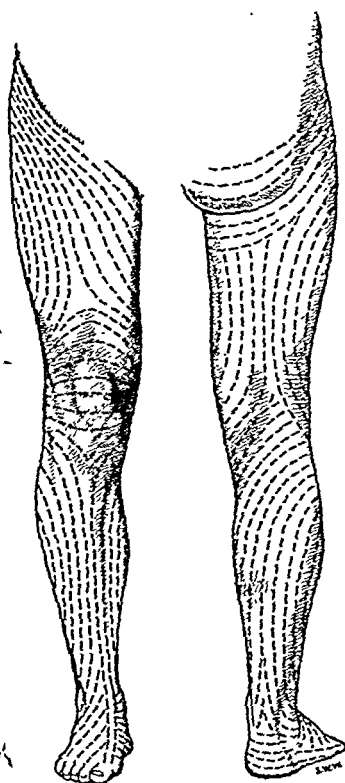


FIG. 5

FIG. 5.—The lines of incision which are most beneficial to the patient so far as healing is concerned. This drawing is to demonstrate Langer's lines, first described in 1861. It is important in this operation to take advantage of the help these lines can give, since the patient is ambulatory and no strain during exercise which can be avoided should be admitted.

FIG. 6.—Some of the varied methods of termination of the internal saphenous vein and its tributaries. These diagrams are copied from those described by Daseler *et al.* (1946), and are the result of extensive investigations on both cadavers and patients. These varied methods of entry of the tributaries of the internal saphenous vein show that few cases subjected to operation prove to be similar. Tortuosities and saccular dilatations may occur in the branches, causing them to be even more prominent than the internal saphenous vein itself.

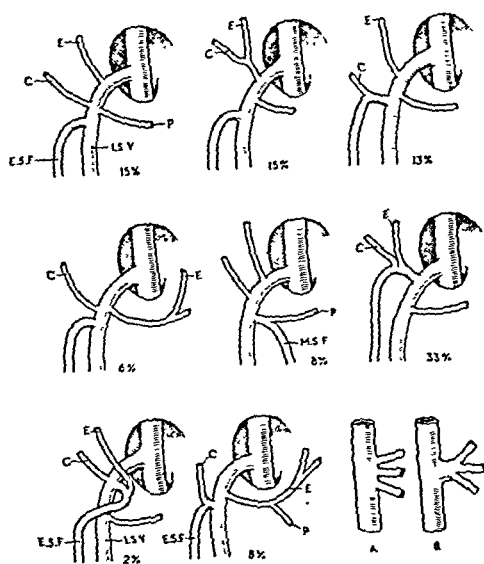


FIG. 6

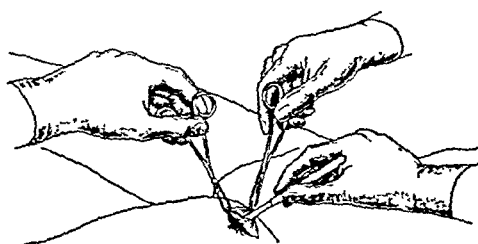


FIG. 7

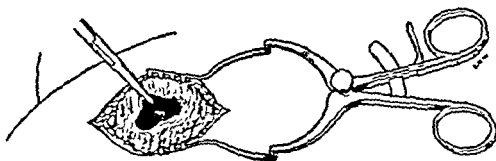


FIG. 8

FIG. 7.—This diagram emphasizes that careful lifting of the tissues once the superficial fascia has been incised is important. By this method the saphenous vein is made to fall away from the fat and subcutaneous tissue and the knife can be used until the vein is actually exposed to view intact. The knife should not be dropped until the vein is seen. Otherwise the fat and subcutaneous tissues may be pushed over the vein and the search prolonged.

FIG. 8.—The vein is exposed and a special self-retaining retractor (Bell and Croyden) is placed in the wound. This retractor has semi-blunt points which cannot damage the important adjacent vessels and it is so constructed that it lies flat, out of the surgeon's way. Note that when grasping the vein a firm bite should be taken. Nibbling at the vein may cause it to rupture.

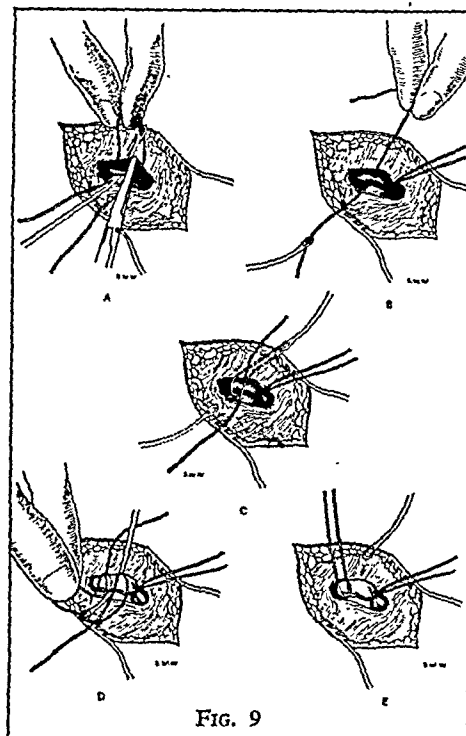


FIG. 9

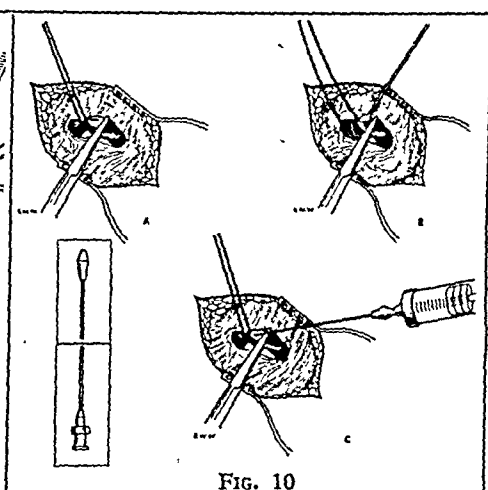


FIG. 10

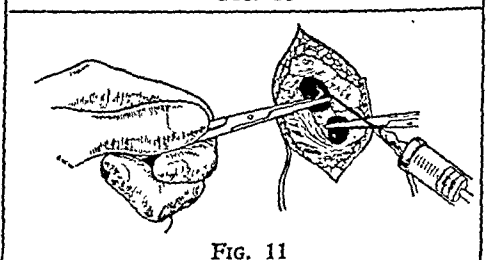


FIG. 11

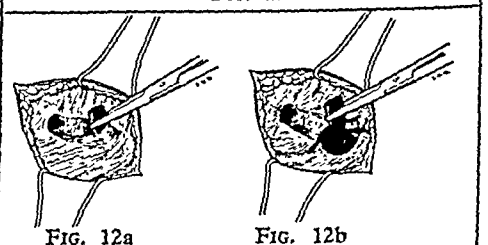


FIG. 12a

FIG. 12b

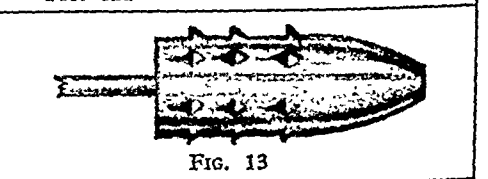


FIG. 13

FIG. 9.—Showing the proximal end of the saphenous vein either clamped or ligated. The operator is now interested in the distal portion of the saphenous vein around which he is placing a slip ligature. Details of how this is done with an aneurysm needle is shown. It should be noted that it is the top thread which is finally pulled through before the aneurysm needle is removed.

FIG. 10.—The slip ligature being pulled taut and the vein being sufficiently incised to allow the head of the Stevenson's needle or one of its modifications, to be inserted. As the head is pushed into the lumen of the vein the slip ligature is relaxed and only tightened again when the head has passed into the vein. In this way no blood loss or escape of sclerosant should be allowed. This illustration shows the use of a smooth-headed needle. I have a preference for my roughened adaptation of this needle which causes damage to the delicate intima of the vein and produces better thrombosis with a lessening in the amount of sclerosant used (see fig. 13).

FIG. 11.—The injection of sclerosant fluid into the distal portion of the internal saphenous vein by means of a record syringe fitted with a wide-bore sharp needle. This method is quicker and in some hands more simple. Whether it is as efficient as when using the Stevenson's needle is debatable. When using this method a clock-wise rotation of the clamp aids in the insertion of the needle.

FIG. 12a.—The distal portion of the internal saphenous vein has been ligated and transfixed. The stripping-up process of the proximal stump causes a thick fold of fascia to appear. When operating under local anaesthesia careful sharp dissection prevents discomfort to the patient. Fine strabismus scissors are of value in this part of the operation.

FIG. 12b.—The internal saphenous vein has been exposed up to its junction with the femoral vein. Branches are better ligated by means of an aneurysm needle and fine thread rather than by artery forceps which tend to obscure the field of operation.

FIG. 13.—The modified head of the Stevenson's needle (see fig. 10).

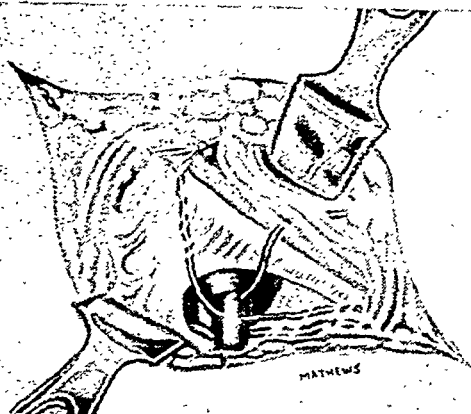


FIG. 14

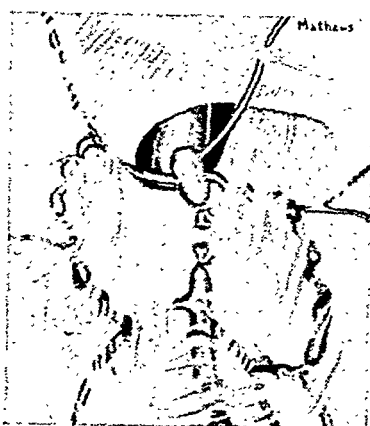


FIG. 15

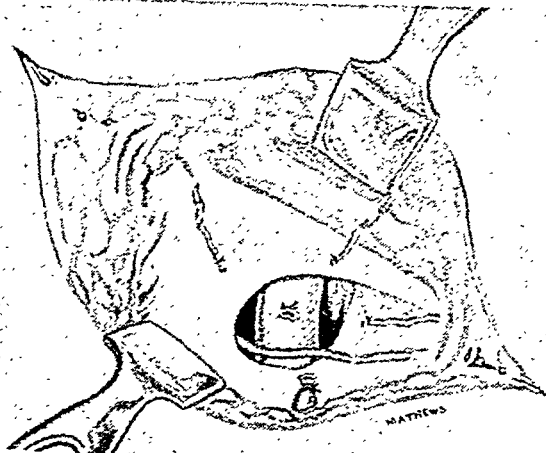


FIG. 17



FIG. 16

FIG. 14.—Another view of the internal saphenous vein at its termination. Note the position of the femoral vein, the superficial circumflex iliac vein, the superficial epigastric vein and the superficial external pudendal vein. The external pudendal artery is occupying its most usual position crossing the femoral vein deep to the internal saphenous vein at the sapheno-femoral junction. In ten per cent. of cases this artery lies anterior to the internal saphenous vein.

FIG. 15.—A common fault in varicose vein surgery. Neglect to ligate tributaries has caused the by-passing of the main stem and recurrence has taken place through anastomosing channels.

FIG. 16.—Possible further mistakes at the saphenous opening. The upper diagram demonstrates low ligation of the internal saphenous vein. Recurrences are inevitable from such slovenly surgery. The lower diagram shows the ligation of the lateral superficial femoral vein instead of the internal saphenous vein. This mistake, surprisingly enough, is not at all uncommon and naturally does nothing to improve the patient's condition.

FIG. 17.—The completion of the operation. A "flush tie" has been performed, all branches have been ligated and the wound is now ready for suture.

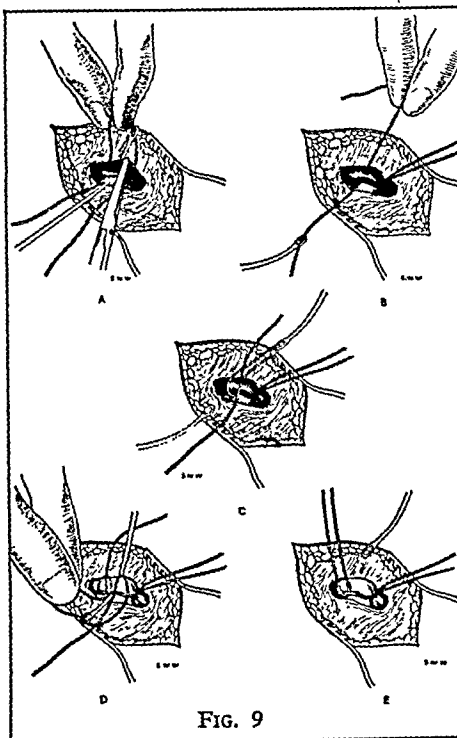


FIG. 9

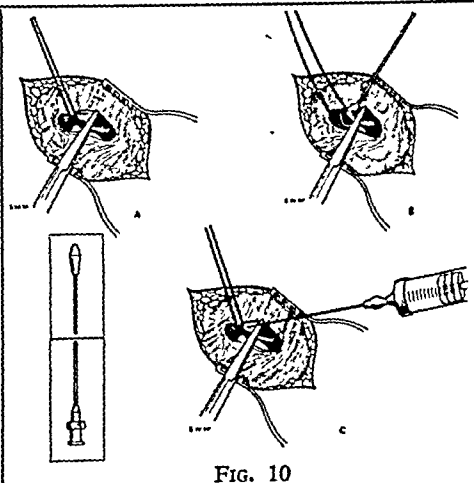


FIG. 10

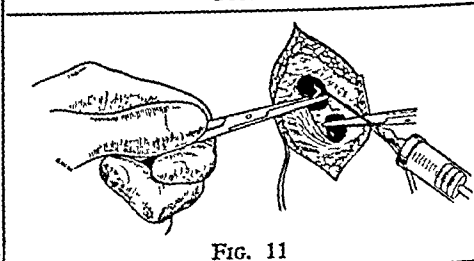


FIG. 11

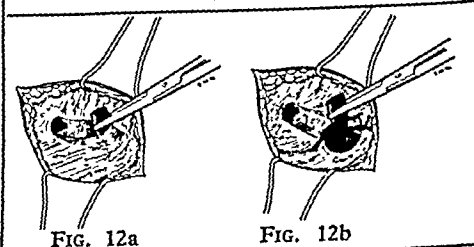


FIG. 12a

FIG. 12b

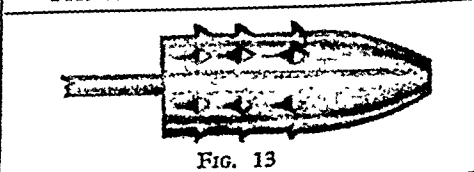


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These figures call for some explanation. Assuming that the verdicts were correct—and coroners are properly cautious in this direction—the 486 persons referred to above did, in fact, put an end to their lives by the methods indicated. But it would be wrong to suppose that this figure represents the total number of suicides in the area during the period under discussion. The true figure would quite certainly be higher. It must be remembered that, in the absence of proof to the contrary, there is, in law, a presumption *against* suicide. In a number of cases reported and investigated as probable suicides the evidence will be quite insufficient to establish the necessary proof and the coroner will return an open verdict.

In many cases, whatever the means adopted, the evidence is complete and convincing and affords no grounds for doubt. Although persons who take their lives often do so in conditions of privacy that may exclude the possibility of direct visual evidence of their acts, they frequently leave behind them notes or letters signifying their intentions. Such notes and letters are admissible on proof that they are in the deceased's handwriting, and are often valuable links in the chain of evidence. The direct testimony of relatives and friends as to the deceased's death, habits, temperament, and recent demeanour is of great importance, as are facts relating to domestic and economic circumstances, mental and psychical peculiarities, and previous attempts at suicide. When evidence of this sort is available the coroner's task is often an easy one.

But there are instances in which no suicide note is left and no one appears to know much about the deceased, and, in fact, evidence of the kind outlined above is partly or wholly lacking. In such cases a considerable degree of uncertainty is likely to arise. The extent of such uncertainty will depend largely upon the means of suicide adopted. Difficulties are especially likely to arise in two classes of cases, i.e. deaths by drowning and those resulting from falls from heights.

COAL-GAS POISONING

As the tabulated figures indicate, this is by far the most commonly practised method of suicide in urban areas. Men and women equally avail themselves of the facilities presented by the domestic gas supply for ensuring an easy and painless means of self-destruction. Nearly everyone is familiar with the fact that such attempts rarely fail. There is, moreover, generally an opportunity to carry out the act without arousing the suspicion of other members of the household.

The procedure adopted is nearly always the same; indeed, it may be said that it usually conforms to an accepted ritual. Windows and doors are shut or sealed; the gas-oven is opened and the metal trays removed; a pillow is put in position to support the head and a rug or eiderdown placed over the mouth; the taps are turned on and the victim rapidly sinks into unconsciousness and death. A note is often discovered on the dresser or kitchen table, and the last act of many of these unfortunate people is to pin a notice on the outside of the door warning those who may be about to enter of the presence of escaping gas.

METHODS OF SUICIDE

By W. R. H. HEDDY, M.R.C.S., L.R.C.P., D.P.H.

Coroner for the Eastern District County of London.

METHODS of committing suicide have varied to some extent from age to age. An examination of early records shows that hanging, drowning, and the infliction of wounds were common methods of self-destruction in mediæval times. The would-be suicide could always improvise a self-made halter; he could without difficulty immerse himself in the village pond or jump into the castle moat. He could leap from the tower of the neighbouring church or wound himself fatally with one of the singularly formidable domestic knives of the period. If he tried to poison himself the position was less easy, for popular acquaintance with the properties of noxious substances was extremely limited, and attempts in this direction involved trespassing on the preserves of those who practised the magic arts. Nor, until firearms became relatively precise weapons, was there much attraction in the prospect of attempting to shoot oneself. There were no lethal vehicles in front of which to dive with prospects of success. There was no handy supply of domestic coal-gas to furnish an easy way of putting an end to an insupportable existence.

Suicide methods, then, if they do not vary much from decade to decade, certainly change from generation to generation. In the Eastern District of the County of London during the period January 1940 to December 1947 suicide verdicts were returned in 486 cases. The means adopted and the proportion of men to women in each category are indicated in table 1.

TABLE 1

Means	Males	Females	Total
Coal-gas poisoning ..	89	75	164
Drowning	55	23	78
Poisons	35	34	69
Hanging	51	8	59
Jumps from heights ..	17	14	31
Cut throats and other self-inflicted wounds ..	23	6	29
Jumps in front of vehicles	17	11	28
Firearm wounds	20	Nil	20
Drugs in poisonous doses ..	3	5	8
Totals	310	176	486

These figures call for some explanation. Assuming that the verdicts were correct—and coroners are properly cautious in this direction—the 486 persons referred to above did, in fact, put an end to their lives by the methods indicated. But it would be wrong to suppose that this figure represents the total number of suicides in the area during the period under discussion. The true figure would quite certainly be higher. It must be remembered that, in the absence of proof to the contrary, there is, in law, a presumption *against* suicide. In a number of cases reported and investigated as probable suicides the evidence will be quite insufficient to establish the necessary proof and the coroner will return an open verdict.

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Such cases do not present difficulties, but problems may well arise when the deceased is discovered in a natural position lying on a bed or sitting on a chair in a room filled with gas escaping from taps that have been left on, but otherwise presenting no signs of preparation for suicide. Still more puzzling are the cases occasionally met with in which the deceased is found suffering from the effects of carbon monoxide poisoning in a room in which the gas taps are in the *off* position. It may be mentioned in passing that cases of accidental poisoning by coal-gas are more common than is generally supposed. The source of the poisonous fumes is not always within the room or even within the house. It is sometimes very difficult to detect. In two cases that came to my notice individuals were fatally poisoned by escaping gas which had seeped through into the basement rooms of dwelling houses situated a considerable distance away from a leaking main.

The practitioner should remember that revival after exposure to carbon monoxide poisoning does not necessarily indicate recovery from the condition. Prognosis should be guarded in view of the possibility of death from softening of the basal nuclei at a later stage.

DROWNING

Suicide verdicts were returned in the cases of 55 men and 23 women who were found drowned, either in the main stream of the River Thames, its tributary canals, or the waters of its docks. In many of these cases the deceased persons either left letters announcing their intentions or had spoken to others of their determination to put an end to their lives. In some cases, although direct evidence of intention was lacking, there was a history of altered demeanour or strange behaviour sufficiently marked to arouse the anxiety of relatives and friends. When such persons slip out of their homes at unlikely hours, unbeknown to their relatives, and are subsequently found drowned in a canal a few streets away in circumstances that seem to negative the idea of accidental immersion, the evidence may be sufficient to justify a suicide verdict. But when the body of a person is recovered from the main stream of the river or the waters of a dock and there is merely a vague history of moodiness and depression the position is entirely different. Open verdicts are commonly and properly returned in such circumstances, although there can be little doubt that many are, in fact, cases of suicide.

The practitioner who is called upon to examine a body recently recovered from the water is sometimes asked for his opinion as to the period of immersion. He should frame his answer in such a way as to give himself the widest latitude. Many bodies fail altogether to conform to the requirements of the textbooks. There are so many factors that may interfere with the classical interpretations that it is wise to be most guarded. It is even more dangerous to hazard an opinion as to how and where a body may have drifted with the ebb and flow of the tide.

Hanging as a method of suicide is still very common. But, as a reference to table 1 will show, it is a method employed by men (51) far more often than

by women (8). The preparations are, as a rule, of a simple nature, the individual making use of a piece of rope or cord which is attached to some convenient point of suspension and used as a ligature to constrict the neck when the weight of the body is allowed to depend from it.

Death is usually, though not invariably, due to asphyxia. It occasionally results from vagal inhibition or cerebral anoxia. When more elaborate arrangements have been employed, and especially when complicated systems of straps and buckles have been introduced, the possibility of a masochistic experiment must be borne in mind. These cases, which are not uncommon, are most important from the coroner's point of view. An assessment of all the circumstances may suggest the absence of any suicidal intent and the resulting verdict may be one of misadventure.

CUT THROATS AND OTHER SELF-INFLICTED WOUNDS

Cut throat.—This method of suicide also is far more commonly adopted by men (23) than by women (6). Preliminary cuts of a tentative nature are frequently made before the subject accomplishes the stroke that proves fatal. This is usually made across the throat in the midline, often practically from ear to ear, an open razor or a sharp knife being the instrument of choice. Death may follow rapidly from arterial or venous bleeding: occasionally the incision is of such a determined character that practically all the structures of the neck are severed. The differentiation between self-inflicted and incised homicidal wounds of the throat is one of the classical set-pieces of medical jurisprudence.

Stab wounds may offer more difficult problems. In distinguishing between the suicidal and homicidal type considerable importance attaches to the site of the injury. Suicidal stab wounds of the heart are relatively common; it is remarkable how often individuals with (presumably) no knowledge of anatomy succeed in penetrating this organ, often with weapons singularly unsuitable for the purpose.

Severed arteries.—Among the suicide failures are the fairly frequent cases of old people who unsuccessfully endeavour to sever the radial artery by means of a few feeble scratches with discarded safety-razor blades.

JUMPS FROM HEIGHTS

It may be argued that people rarely fall out of windows in a purely accidental fashion. If they are in good health, and are sober, and are in full possession of their faculties, they seldom do. But when these conditions are not fulfilled experience shows that people can and do fall from windows without any deliberate intention of putting an end to their lives. The drunken sailor who rushes to his cubicle window in a seamen's hostel to vomit or urinate and climbs on to a chair to effect his purpose may crash to the street below without having had the slightest intention of committing suicide. The sufferer from asthma or hypertension, in a desperate attempt to obtain relief from his symptoms, may fling open the window and lean out, re-

gardless of the fact that he may be placing himself in a position of extrem danger. Possibilities such as these have always to be borne in mind, especially in view of the fact that people who practise this method of suicide seldom leave letters announcing their intentions. These cases are often of the impulsive type and not infrequently take place in the early hours of the morning.

JUMPS IN FRONT OF VEHICLES

Twenty-eight people, seventeen men and eleven women, put an end to their lives by jumping in front of moving vehicles, usually approaching trains (21), less commonly road vehicles (7). Railway suicides generally take the shape of deliberate leaps from the edge of the platform in front of the train as it draws into the station. The evidence of the driver as to the deliberate nature of the jump is usually supported by that of other witnesses. People on the platform may have had their attention drawn to the deceased by a certain oddity of demeanour or behaviour immediately before the suicidal act. Intending suicides often purchase a ticket at their home station for a destination a few miles down the line. There they alight, and often without giving up their ticket, hang about the station precincts until the arrival of another train. This is the most common method of committing suicide on the railway. Sometimes, however, people deliberately lie down in the four-foot way and wait for a train to run over them.

Much more difficult are cases in which it is alleged that the deceased person committed suicide by throwing himself in front of a road vehicle. Only seven of the four hundred and eighty-six persons dealt with in this series made an end of themselves in this way. Most would-be suicides presumably consider the method too uncertain: if so, they are perhaps paying an unconscious tribute to the alertness and resource of bus and tram drivers. Difficulties sometimes arise through the ill-advised but sympathetic comments of excited witnesses who have seen the circumstances of a traffic accident and are convinced that no possible blame can be attributed to the driver. In this supposition they may be entirely correct. But when they let slip such an unguarded phrase as "Suicide, I call it!" intending only to imply that the fault was entirely that of the pedestrian, they may unknowingly be influencing the driver to give an account of the facts that is not entirely true. So erratic is the behaviour of some pedestrians, especially when under the influence of alcohol, that the suggestion of suicide should be received with great reserve.

FIREARMS

Suicide by shooting is a method practised almost exclusively by men. It appeals particularly to those familiar with guns and revolvers and is the method of choice of commissioned officers, rural sportsmen, and retired pensioners from the Services. There are certain classical sites of election—the temple, the brow, the roof of the mouth and, of course, the region of the heart. Suicidal firearm wounds can usually be distinguished from those of a

homicidal nature by a general consideration of the detailed pathological findings, aided in appropriate cases by the expert evidence of the gunsmith. The most difficult cases are those in which death occurs while the deceased is handling a weapon, conceivably with the intention of adjusting or cleaning it.

POISONS

As table 1 indicates, both men (35) and women (34) make use of this method. Fifty years ago the figures under this heading would undoubtedly have been higher. The method is still favoured by the acutely distraught, the poorly educated, and the mentally deranged. The suicidal act is most commonly accomplished by the swallowing of crude disinfectant. A minority of the victims in this series took such substances as prussic acid, oxalic acid, nicotine, and spirits of salts. Efforts of this kind are by no means invariably successful and are often followed by subsequent suicidal acts.

When death has occurred through the swallowing of a substance the noxious qualities of which must be obvious, the facts generally speak for themselves; nevertheless, I can recall a case in which the deceased swallowed without apparent perturbation a considerable quantity of crude phenol that had been handed to him in error by a pharmacist to whom he had applied in perfect good faith for a bottle of "phenol cough mixture".

Drugs in poisonous doses.—Only eight persons in this series adopted this method of suicide. This may appear surprising when it is appreciated that this heading includes those who deliberately took lethal doses of barbiturate drugs. But the explanation is a simple one. Fatal cases of barbiturate poisoning, from whatever cause, are far less commonly met with in the East End of London than in other parts of the capital. The local population is not, to use an overworked phrase, barbiturate-conscious, and the suicide figures are probably not typical of the state of affairs elsewhere.

THE SUICIDE VERDICT

Considerable discussion, much of it ill-informed and unprofitable, has centred round the wording of the verdict in suicide cases. So long as suicide—*felo de se*—remains a felony in law coroners will naturally, when possible, word the verdict in such a way as to divest it of its felonious attributes. Afflicted members of the family are quick to appreciate the charitable implications of a verdict worded to show that the deceased took his life "while the balance of his mind was disturbed". It generally happens to be the truth. In any event, words that bring a measure of solace at a moment of tragedy ought not to be lightly disregarded. The Departmental Committee of 1935, whose report failed to recognize that a spirit of sympathetic understanding is essential to the successful working of these courts, recommended that the verdict should state baldly that the deceased "died by his own hand". It is questionable if grief-stricken relatives would regard the invariable use of this harsh phrase as an improvement on existing practice.

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DOSAGE

Thiouracil is rapidly absorbed and rapidly excreted in the urine. When 0.2 gm. is given three times a day an equilibrium between blood and urine is attained in about forty-eight hours and no increased effect is produced by giving larger doses. This is therefore the initial dose commonly employed, although some workers believe it to be larger than is necessary. This dose is generally given for three weeks to a month, by which time significant effects have usually been produced, and the dose is then reduced to a maintenance one.

Just as in the case of digitalis, the maintenance dose, sufficient to maintain the optimum effect but not to produce signs of overdosage, will vary from patient to patient. A severe case will require about 0.2 gm. a day, whilst milder cases may be maintained by 0.1 gm. a day.

After all thyrotoxic signs and symptoms have been in abeyance for some months a further reduction in dosage can be attempted to 0.1 and finally to 0.05 gm. a day, although a recrudescence of symptoms will necessitate an appropriate increase. If, after three or four months on 0.05 gm. a day, there has been no return of thyrotoxicosis, a trial may be made of stopping the administration of the drug altogether, but relapse is extremely common if treatment has not been continued for at least a year.

CLINICAL EFFECTS

The effects of thiouracil in thyrotoxicosis are on the whole fairly precise and predictable. After a latent period of about ten days or a fortnight some subjective improvement occurs, the sweating and flushing of the skin being usually the first signs to be ameliorated. Thereafter all the signs and symptoms steadily improve, the improvement being significant in three to four weeks, when the dose is reduced to a maintenance one, and maximal in two or three months, when even patients who have been initially severely ill are usually fit to return to work. Mild cases may be treated from the beginning as ambulant patients sometimes without interruption to their employment. The objective and measurable signs of thyrotoxicosis parallel in their improvement the subjective sensations of the patient.

The blood cholesterol.—The blood cholesterol concentration tends to be low in untreated thyrotoxicosis just as it is high in myxœdema. On the average it rises under the influence of thiouracil, but this rise is too variable in individual cases to make estimations of the blood cholesterol concentration a reliable index for the control of treatment.

The basal metabolic rate.—After a latent period of about ten days a fall in the B.M.R. becomes noticeable, which reaches significant proportions in about a month's time. The determination of the B.M.R., however, lacks universality of application in ordinary practice. It is a procedure which is difficult to carry out and unless considerable skill is exercised in the preparation of the patient and in carrying out the test most fallacious results may be attained. In the control of a case by thiouracil it is far better to

CURRENT THERAPEUTICS

V.—THIOURACIL

By D. M. DUNLOP, M.D., F.R.C.P.Ed., M.R.C.P.

Professor of Therapeutics and Clinical Medicine, University of Edinburgh; Physician, Royal Infirmary, Edinburgh.

THIOURACIL has now been in general use for over four years. We are not yet in a position to dogmatize as to its ultimate position in therapeutics but the indications and contraindications for its employment are gradually crystallizing. The over-enthusiasm with which some of us hailed it as the philosopher's stone of treatment in almost all cases of hyperthyroidism has had to be modified; on the other hand the belief held by some, that it should never be used except in the preparation of a patient for thyroidectomy, is much too extreme a view.

PHARMACOLOGICAL ACTION

The derivatives of thiourea are the most active and least toxic of a large number of goitrogenic substances which inhibit the formation of the thyroid hormone by preventing the iodination of tyrosine—the precursor of thyroxine. In consequence, if large doses are given for a sufficient length of time myxœdema is produced. As the result of the myxœdematous state the anterior pituitary is stimulated to produce an excess of thyrotropic hormone which causes the formation of a hyperplastic goitre from which, however, no thyroxine is secreted. The length of time which it takes to produce myxœdema in this way depends to some extent on the dose of anti-thyroid substance used, but more especially on the stores of thyroxine possessed by the gland. In a healthy person it takes a long time—about two months—to produce myxœdema, since the healthy thyroid contains a large store of thyroxine in the colloid of its follicles. Since, however, the store of thyroid hormone in hyperthyroid glands is greatly decreased some effect is produced by thiouracil in thyrotoxic cases in about a fortnight. The aim of treatment in thyrotoxicosis is to reduce the synthesis of thyroxine to a normal level and by a maintenance dose to maintain the optimum level of metabolism, avoiding over-dosage which will cause myxœdema and an increase in the size of the goitre.

PREPARATIONS

Thiourea itself is now seldom used; it is unpleasant to take and is more toxic than thiouracil or methyl thiouracil. It has been claimed on inadequate evidence that the latter is less toxic than thiouracil. There is probably little difference between the two either in their efficiency or toxicity, but as methyl thiouracil is a little cheaper than thiouracil it is the preferable drug. The new preparation, propyl thiouracil, is stated to be less toxic than any of the other drugs and to be effective in much smaller dosage. So far the clinical trials of this substance have been insufficient to substantiate these claims.

DOSAGE

Thiouracil is rapidly absorbed and rapidly excreted in the urine. When 0.2 gm. is given three times a day an equilibrium between blood and urine is attained in about forty-eight hours and no increased effect is produced by giving larger doses. This is therefore the initial dose commonly employed, although some workers believe it to be larger than is necessary. This dose is generally given for three weeks to a month, by which time significant effects have usually been produced, and the dose is then reduced to a maintenance one.

Just as in the case of digitalis, the maintenance dose, sufficient to maintain the optimum effect but not to produce signs of overdosage, will vary from patient to patient. A severe case will require about 0.2 gm. a day, whilst milder cases may be maintained by 0.1 gm. a day.

After all thyrotoxic signs and symptoms have been in abeyance for some months a further reduction in dosage can be attempted to 0.1 and finally to 0.05 gm. a day, although a recrudescence of symptoms will necessitate an appropriate increase. If, after three or four months on 0.05 gm. a day, there has been no return of thyrotoxicosis, a trial may be made of stopping the administration of the drug altogether, but relapse is extremely common if treatment has not been continued for at least a year.

CLINICAL EFFECTS

The effects of thiouracil in thyrotoxicosis are on the whole fairly precise and predictable. After a latent period of about ten days or a fortnight some subjective improvement occurs, the sweating and flushing of the skin being usually the first signs to be ameliorated. Thereafter all the signs and symptoms steadily improve, the improvement being significant in three to four weeks, when the dose is reduced to a maintenance one, and maximal in two or three months, when even patients who have been initially severely ill are usually fit to return to work. Mild cases may be treated from the beginning as ambulant patients sometimes without interruption to their employment. The objective and measurable signs of thyrotoxicosis parallel in their improvement the subjective sensations of the patient.

The blood cholesterol.—The blood cholesterol concentration tends to be low in untreated thyrotoxicosis just as it is high in myxædema. On the average it rises under the influence of thiouracil, but this rise is too variable in individual cases to make estimations of the blood cholesterol concentration a reliable index for the control of treatment.

The basal metabolic rate.—After a latent period of about ten days a fall in the B.M.R. becomes noticeable, which reaches significant proportions in about a month's time. The determination of the B.M.R., however, lacks universality of application in ordinary practice. It is a procedure which is difficult to carry out and unless considerable skill is exercised in the preparation of the patient and in carrying out the test most fallacious results may be attained. In the control of a case by thiouracil it is far better to

rely on the clinical signs and symptoms of the patient than on estimations of the blood cholesterol and determinations of the B.M.R.

The weight.—A gain in weight is a characteristic effect produced by thiouracil. On the average the weight increases steadily during the first few months of treatment, and is often a very striking and, in patients not originally underweight, even an embarrassing result. Patients under treatment should be weighed regularly: in active cases an increasing weight is a valuable sign of improvement; in quiescent cases a stationary weight is equally reassuring; in all cases a fall in weight of even a few pounds, especially if steadily maintained, is disquieting and is a signal for a review of the whole treatment of the case.

The heart.—Thiouracil does not act uniformly on all the signs of thyrotoxicosis, and the last to show improvement is often the associated tachycardia and high pulse pressure. When a marked degree of tachycardia and high pulse pressure exists, their control may be delayed long after the other signs and symptoms have greatly improved. Thyroidectomy undoubtedly produces a more dramatic immediate effect on tachycardia than thiouracil, and its ultimate effect on the thyrotoxic heart may also be superior—an argument in favour of surgery in secondary nodular goitre which is particularly characterized by circulatory disabilities.

In a few cases thyrotoxic auricular fibrillation returns spontaneously to normal rhythm under the influence of thiouracil, just as normal rhythm may occur spontaneously after thyroidectomy. Fibrillation, however, commonly persists in spite of the satisfactory control of the other features of hyperthyroidism by thiouracil, and treatment with quinidine may be necessary to restore normal rhythm. The literature suggests that thyroidectomy is more effective than thiouracil in this respect, but there is little reference in it to the combined use of thiouracil and quinidine, which is usually most successful, whereas quinidine is frequently employed following thyroidectomy.

Exophthalmos is not materially affected by thiouracil. Some slight improvement in this feature may occur after prolonged treatment, but on the average, thyroidectomy is more likely to diminish exophthalmos, although in many cases it may be equally ineffective.

The goitre.—On the whole, also, thiouracil does not greatly diminish the size of the goitre. This constitutes a definite disadvantage when the goitre is large and disfiguring or if there is any tendency to pressure symptoms, particularly if the goitre is retrosternal in position. On the other hand when the goitre is small it is less cosmetically disfiguring than some of the scars produced in the neck by thyroidectomy. Occasionally the gland becomes definitely smaller as the result of treatment by thiouracil, particularly in cases in which the thyrotoxicosis has been abolished for a long time and it has been possible to discontinue the use of the drug. The goitre always becomes softer under the influence of thiouracil, in contrast to the firmer gland produced by treatment with iodine.

Whereas the effect of thiouracil in diminishing the size of the gland is not very dramatic there can be no doubt that overdosage may greatly increase the size of the goitre by causing myxœdema with a consequent over-production of thyrotrophic hormone. Such myxœdema is, however, purely temporary if the administration of the drug is stopped for a while, in contrast to the permanent myxœdema which occurs in about four per cent. of cases following thyroidectomy.

Pregnancy.—There is no contraindication to the use of thiouracil when pregnancy complicates hyperthyroidism. I have treated successfully numerous thyrotoxic pregnant women with the drug without untoward effects upon the baby.

Drug resistance.—Resistance to thiouracil is seldom encountered, but occasionally the response to treatment is unsatisfactory. In the majority of such cases it will be found that the psychological rather than the endocrine factor is proving the more important.

TOXIC EFFECTS

Like most potent modern drugs thiouracil is a two-edged weapon and will produce toxic reactions in about twelve per cent. of cases, sufficiently serious in over half of them to necessitate termination of treatment. It is most important that the practitioner should be familiar with these toxic effects before using the drug. The side-effects are, in increasing order of seriousness, swelling of the legs and feet, conjunctivitis, enlargement of lymph glands, rashes, pyrexia, vomiting, and blood dyscrasias such as leucopenia, thrombocytopenia, purpura and agranulocytosis. Of these, the serious signs calling for immediate cessation of treatment are pyrexia, vomiting, the blood dyscrasias and occasionally troublesome skin rashes. The other toxic manifestations are usually transient and trivial—the slight œdema of the feet and ankles which may occur being unassociated with cardiac or renal damage. It disappears in spite of the continuation of treatment.

Toxic reactions, especially the blood dyscrasias, are most likely to occur during the first month of treatment, when the patient is taking a full dose of the drug, and are less common later on. It is thus no doubt ideal during the initial stage of treatment to perform white blood counts on the patient every three days. This is, however, a council of perfection, quite impracticable outside hospital, and unless the hæmatological examinations are very frequent they are of no avail in giving warning of the imminence of agranulocytosis which may be extremely sudden in onset. Therefore in ordinary practice it is sufficient to give the patient detailed instructions to stop taking thiouracil and to report at once should he feel ill, and especially if skin rashes, vomiting, fever or sore throat manifest themselves.

A mortality of about 0.5 per cent. from toxic effects has been recorded in the literature. This figure should be greatly lessened in the future as knowledge of the toxic reactions to the drug becomes more widespread. In addition, most of the fatalities occurred from agranulocytosis before the

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Thiouracil is definitely contraindicated when the goitre is retrosternal or when pressure symptoms exist.

Lastly, there are some patients—usually not in the hospital class—whose goitre and thyrotoxic state have become almost an obsession and who dislike the idea of continuing to take a drug for a long time without the certainty that it will ultimately cure them. Such patients may express a strong preference to have their goitre removed once and for all. Provided the case is not one of mild primary thyrotoxicosis in a young girl the patient is entitled to her choice. On the other hand, patients recommended to have a thyroidectomy may be adamant in their refusal to undergo an operation. For such, thiouracil provides an alternative method of satisfactory therapy.

PREOPERATIVE TREATMENT

Operations such as appendicectomy and tonsillectomy may be successfully undertaken on a thyrotoxic patient who has been brought fully under the influence of thiouracil, and it is undoubtedly a superior drug to iodine for such purposes. Considerable controversy has existed, however, as to the relative merits of iodine and thiouracil in the preoperative preparation of a patient for thyroidectomy. Each has its advantages and disadvantages. Iodine seldom completely restores the metabolism of a severe case to normal and, although it greatly improves thyrotoxic signs and symptoms, it only ameliorates them to a greater or less extent and does not hold them in complete abeyance as is usually the case with thiouracil. Thus the pulse rate tends to be more rapid during the operation, and postoperative thyrotoxic crises may be more common in patients prepared by iodine than in those prepared by thiouracil. On the other hand there is no doubt that the thyroids of patients prepared for thyroidectomy by thiouracil are more vascular than those prepared by iodine, and in consequence the operation may be made more difficult and hazardous owing to intractable hæmorrhage. Further, owing to the leucopenic effect of thiouracil, it has been claimed that postoperative infections are more common following its use.

It is probably wise therefore to make use of both drugs in the preparation of a patient for thyroidectomy: thiouracil should be given until all thyrotoxic signs and symptoms are well controlled; its administration is then discontinued and iodine is given for the ten days immediately before operation. In this way the advantages of both drugs are secured and their disadvantages minimized. Using this preoperative technique the mortality from thyroidectomy—already well under two per cent. in the hands of experts—should be still further reduced.

effectiveness of penicillin in the treatment of that condition was generally recognized.

ULTIMATE EFFECTS

It is as yet too early to dogmatize on the ultimate effects of thiouracil treatment. It should certainly be continued for at least a year and often for longer. If treatment is terminated before that time a large proportion of cases relapse. Further, it is unwise to stop the administration of the drug unless thyrotoxic signs and symptoms have been kept in complete abeyance for several months by as small a dose as 0.05 gm. a day. There are strong grounds for believing that ultimate complete cure may result in a considerable proportion of cases of primary thyrotoxicosis from long continued treatment. From previous experience it is known that many young girls suffering from hyperthyroidism recovered spontaneously, particularly if a satisfactory solution was found to domestic worries, unhappiness at work or an affair of the heart. The use of thiouracil does not liquidate the physician's responsibility to seek for and to try to eliminate psychological stresses and strains. If in addition, however, the psychosomatic vicious circle can be broken for a long time on the endocrine side, strong hopes of permanent remission may be entertained. These hopes are justified by many patients whose thyrotoxicosis has remained in abeyance for more than two years after treatment has been discontinued. A relapse can be controlled by a further course of treatment.

It is more doubtful whether treatment can be successfully terminated in cases of secondary nodular goitre, and this may constitute a justification and indeed an indication for thyroidectomy in such patients. It must not be thought, however, that many of them will not react very well to thiouracil as long as it is being administered.

CHOICE OF TREATMENT

I have no doubt that thiouracil is the treatment of choice in young people with primary thyrotoxicosis, provided that the goitre is not very large and unsightly. It is most undesirable to interfere radically with the endocrine system in such patients, particularly when we know that some of them recover spontaneously and many will recover with wise psychological guidance and with the help of thiouracil. The risks of treatment with thiouracil in such cases are probably less than the operative risks of thyroidectomy, even in the hands of experts, and very much less than the risks of operation undertaken by those not thoroughly experienced in the art of thyroid surgery. If the primary hyperthyroid case develops toxic reactions to thiouracil, or if the results of treatment are in any way unsatisfactory, surgery is always a second line of defence.

Postoperative recurrences of hyperthyroidism should as a general rule be treated by thiouracil in preference to further surgery.

Thyroidectomy on the other hand is the treatment of choice for middle-aged people with toxic adenomatous goitres. Although such patients may

benefit greatly from thiouracil, it probably never cures them and has to be continued permanently. Further, it may have less favourable effects than has thyroidectomy on their characteristic circulatory disturbances, and moreover surgical interference with the endocrine system is less objectionable in older than in younger people. Thiouracil treatment, however, is usually preferable to surgery in really old, as opposed to middle-aged people who are suffering from degenerative changes as well as thyrotoxicosis.

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REVISION CORNER

THE TREATMENT OF PROLAPSE

GENITAL prolapse, or "fallen womb", manifests itself in certain well-defined types according to the supporting structures mainly involved. Paradoxically it is more often a vaginal than a uterine condition, although a combination of the two is quite common.

ANATOMY

The anterior vaginal wall is supported by the pubo-cervical sheet of pelvic fascia which runs forwards and slightly downwards from the anterior aspect of the supravaginal cervix to the back of the pubes (fig. 1 and 3). This layer lies between the under-surface of the bladder and the anterior vaginal wall, to both of which it is intimately attached. Damage to this structure results in descent of the anterior

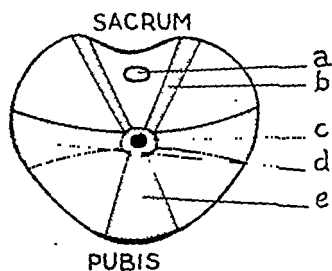


FIG. 1.—(a) Rectum. (b) Utero-sacral ligament. (c) Cervix uteri. (d) Cardinal ligaments (Mackenrodt's). (e) Pubo-cervical fascia.

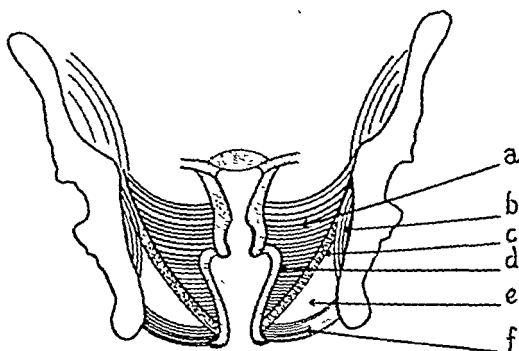


FIG. 2.—(a) Para-cervical tissue and cardinal ligaments. (b) Obturator internus muscle. (c) Levator ani muscle. (d) Para-vaginal tissue. (e) Ischio-rectal fossa. (f) Superficial perineal muscles.

vaginal wall and base of the bladder, producing "cystocele", the most common type of so-called "prolapse".

The cervix uteri rests in a hammock-like structure composed of the two cardinal ligaments (Mackenrodt's) slung transversely

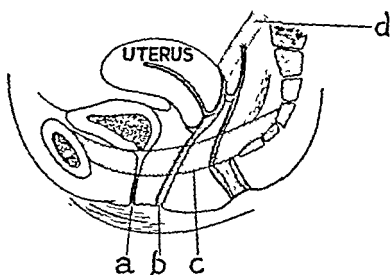


FIG. 3.—(a) Urethra. (b) Vagina. (c) Medial margin of pubo-coccygeus muscle. (d) Utero-sacral ligament.

across the pelvis and permitting limited vertical movement (fig. 1 and 2). From the back of the cervix the thin utero-sacral ligaments run upwards and slightly backwards, passing on either side of the rectum to be attached to the front of the sacrum (fig. 1 and 3). The vaginal vault, firmly attached to the supravaginal cervix, is supported by these same structures. By means of these specialized bands of parametrial tissue and pelvic fascia, the cervix is suspended at its normal level, whilst the body of the uterus is permitted free backward, forward, and lateral movements and is able to accommodate itself to systole and diastole of the bladder as well as to the profound anatomical changes of pregnancy. Faults in these two structures permit excessive descent of the uterus so that the cervix and vaginal fornices appear at or beyond the vulva (true prolapsus uteri).

The lower third of the vagina passes through, and is supported by, the muscular

pelvic diaphragm formed by the levatores ani muscles of either side, reinforced more superficially by the sphincter layer of muscles in the perineum (fig. 2 and 3). Deficiencies in these structures, usually the result of tears or overstretching of the perineum, will affect only the lower one-and-a-half inches of the vagina, producing "urethrocele" and "rectocele" with a gaping vaginal ostium.

ETIOLOGY

Although it is true that occasional cases of "prolapse" are encountered in nulliparæ, parturition is by far the most common etiological factor. Trauma to the canal and its supports during the process of childbearing, and subinvolution of these structures following delivery, are the two elements concerned, and their relative importance may be a matter of some controversy.

All forms of assisted delivery, even low forceps and "after-coming heads", carry a risk of lacerations and overstretching of the pelvic floor, and damage to the cardinal supports of the uterus itself is almost inevitable if such assistance is tendered prematurely by "high forceps", or through an incompletely dilated cervix, or by violent and premature attempts at expulsion of the placenta. On the other hand, to allow a patient to exhaust herself in the first stage by mismanagement or faulty diagnosis to such a degree as to preclude cooperation in the second stage will inevitably increase the necessity for artificial assistance. Again, to leave the patient for an inordinate length of time in the second stage may result in an overstretched vagina, perineum and urethra, which may never completely recover. Timely episiotomy in the primipara, particularly in forceps and breech deliveries, is widely used to avoid this last contingency. In addition, it reduces the necessity for forceps, permits a perfect reconstruction of the pelvic floor, lowers the incidence of "stress incontinence", and relieves dangerous pressure on the foetal skull. Neglect of postural treatment and exercises in the puerperium, as well as failure to treat early retroversions and constipation, will aggravate the tendency to subinvolution, as will also rapidly repeated pregnancies and over-strenuous work.

From these comments it emerges that a considerable number of cases of "prolapse" are fundamentally avoidable. Experience goes to show, however, that there remains a residuum of women with a "lowered modulus of elasticity" whose stretched tissues fail to return to their normal tone despite every known precaution.

TREATMENT

The recent case of prolapse, as a rule manifested by vaginal laxity and slight descent of the cervix and usually discovered at the postnatal examination, should be treated by afternoon rest, plain muscle tonics, sphincter exercises, cold douches, and simple laxatives to avoid constipation. A simple rubber ring pessary is often useful, but its size must be gradually reduced as involution occurs.

The established case, seen months or years after delivery, is treated by some form of plastic operation, and for success careful preoperative preparation is essential. Rest, aperients, sulphacetamide, diluents and alkalis, are required, and a short course of œstrone in post-menopausal cases will prove helpful to good healing. Œdematous and ulcerated cases will usually respond to complete rest, replacement, and antiseptic cleansing for two to four weeks before operation.

In cases of *cystocele*:—

A triangular piece of the anterior vaginal wall and the pubo-cervical fascia is excised as shown in fig. 4, the sides of the triangle being straight or convex, according to the degree of laxity. The bladder is pushed upwards off the front of the supravaginal cervix, and the cut edges of the pubo-cervical fascia are carefully sewn together under the vaginal skin. A final layer of sutures then unites the cut edges of the vaginal wall, and the operation is completed by a posterior colpoperineorrhaphy to strengthen the pelvic floor. This last step does not merely aim at reducing the patulous vaginal ostium; it is also designed to repair the rectocele and to build up a muscular elastic perineum by approximating the inner

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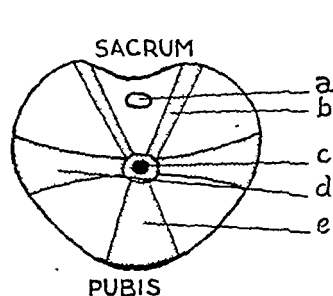


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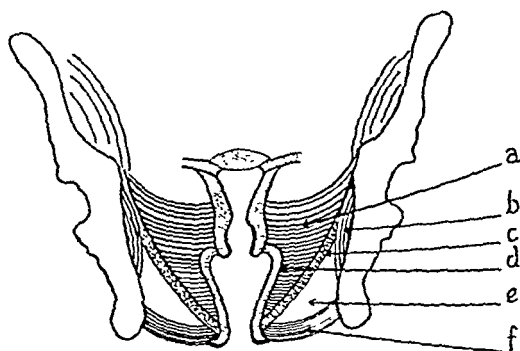


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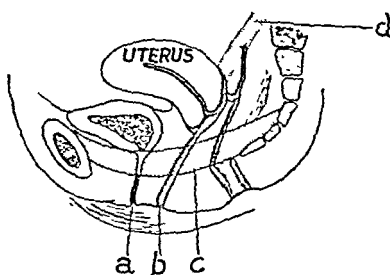


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The lower third of the vagina passes through, and is supported by, the muscular

"interposition" and the obliterative methods of Le Fort. This generally is the fate of operations which grossly distort anatomy and physiology. Rational reconstruction is the present trend—and the results, anatomical and functional, are correspondingly satisfactory.

H. HARVEY EVERS, M.S., F.R.C.S., F.R.C.O.G.

THE TREATMENT OF RINGWORM INFECTIONS

THERE have been no spectacular innovations in the treatment of fungus infection of the skin comparable with the discovery of antibiotics in bacteriology. Nevertheless, the numerous valuable contributions to mycology, both botanical and clinical, the study of which was inaugurated just over a hundred years ago, have made for a better understanding of the pathogenic fungi, and treatment during the last twenty years has benefited accordingly. As treatment of fungus infection cannot be dissociated from other factors, such as detection and identification, it might be best first to discuss it under these headings.

DETECTION

When ringworm fungi attack glabrous skin, they may produce either scaly, discoid patches with a minimum degree of inflammation, or very inflamed rings, sometimes vesicular and also concentric. The former are pathognomonic of the human species of microsporon (*M. audouinii*) and the latter of that conveyed from the cat or dog (*M. felinum vel M. caninum*). Further, owing to the higher degree of infectivity of the latter, the lesions are usually much more numerous. Another less common cause of *Tinea circinata* in this country is *Trichophyton purpureum*, which produces very inflamed, broad rings which, although relatively clear within, present residual inflammatory follicular papules. In a region where larger downy hairs obtain, such as the dorsum of the hands and forearms, keria, taking the form of boggy swellings beset with small follicular pustules, may develop, and such lesions usually result from inoculation with a trichophyton transmitted from infected cattle.

Discoid, scaly patches, usually confluent and developing asymmetrically in the groins, should suggest *Tinea cruris* due to the epidermophyton, but more inflamed patches, at times with vesicular borders, are usually due to *Tinea pedis*, and those with scattered inflamed but non-pustular follicular papules to *T. purpureum*. Not every scaly or vesicular discoid lesion, however, is of mycotic origin and perhaps the affections most commonly misdiagnosed are those of pityriasis rosea and nummular eczema. This pitfall can readily be avoided by the simple microscopical investigation of superficial scalings. The same examination should permit avoidance of the error of treating every intertrigo of the groin or natal fold as one of mycotic origin.

Scaling between the toes is not necessarily due to fungus infection and many of the reports of the high incidence of athlete's foot among students can be attributed to this error. When the epidermophyton invades the toe interspaces it usually affects first the space between the small and next toe, where it produces a scaly patch with a varying degree of inflammation, and the history of the infection appearing on one foot before the other is usually obtained. The affection then invades the adjacent toe interspaces and may develop on the other foot, but the involvement is not necessarily of the same degree. Vesicular or bullous lesions, again most commonly asymmetrical, are suggestive of infection with a more virulent fungus, usually *T. pedis*. The affections readily confused with mycotic infections of the feet are (a) sweat intertrigo, (b) traumatic dermatitis, (c) monilial infection, and (d) pustular psoriasis. All these can be distinguished by the absence of mycelial elements in potash scrapings but, in addition, sweat intertrigo is invariably symmetrical, traumatic

edges of the pubo-coccygeous muscles between the reconstructed posterior vaginal wall and the new lengthened perineum, thus acting as a buttress to the anterior vaginal wall and restoring the vaginal axis to its original plane parallel to the plane of the pelvic brim.

In cases of true *descent of the uterus*, which is usually accompanied by cystocele, the above operation is modified by carrying the base of the triangular flap of the anterior vaginal wall behind the cervix as shown in fig. 5.

After this flap has been dissected up, the cervix is amputated to an appropriate level

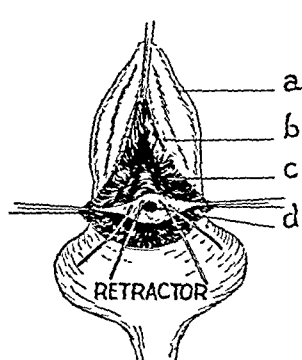


FIG. 4.—(a) Labium minus. (b) Cut edge of vaginal skin and pubo-cervical fascia. (c) Para-cervical tissue. (d) Cervix.

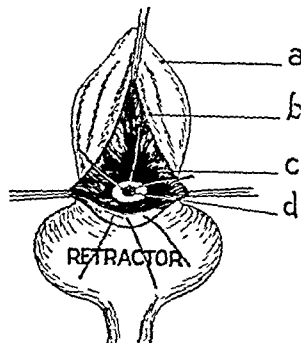


FIG. 5.—(a) Labium minus. (b) Cut edge of cervical skin and pubo-cervical fascia. (c) Para-cervical tissue and cardinal ligaments. (d) Stump of amputated cervix.

through its supravaginal portion, and the cut edges of the base of the triangle are united to the previously dilated cervical orifice as shown also in fig. 5. The next and most vital part of the operation is to unite the fibro-cellular tissue at the sides of the cervix by deep sutures so placed as to pull these cardinal ligaments across the front of the cervical stump in such a way as to shorten them, thereby lifting the cervix upwards and backwards into its normal position. By this means, the coexistent retroversion can frequently be corrected. The operation is completed by suturing the cut edges of the pubo-cervical fascia and of the vaginal skin,

and by performing a posterior colpoperineorrhaphy. These are the principles introduced by Donald and Fothergill, and nowadays generally called the Manchester operation.

In cases of *third degree prolapse* (procentia), when the whole uterus lies outside the contour of the body, it is common practice to combine the Manchester procedure with vaginal hysterectomy in women over forty years of age. In such cases, the cardinal ligaments are obviously cut at the sides just above the vaginal vault, and it is important to unite these by deeply placed sutures to hold up the reconstructed vagina.

If *stress incontinence* is a prominent symptom, special attention is given to the repair of the attachments of the urethra to the back of the pubes. Only a few intractable cases will subsequently require the "fascial sling" operation introduced by Aldridge and Millen.

Scrupulous *after-care* and skilled nursing are essential in all plastic vaginal work. Careful local toilet, urinary antiseptics and test catheterization are especially required. Prolonged rest is not necessary so long as strenuous effort is avoided for six months. Future childbearing, although undesirable, is not contraindicated in most cases, but hospital conduct of the labour with episiotomy is essential.

Age *per se* is rarely, if ever, a contraindication to operation, but those patients with serious cardiovascular disease, poor renal function, and chronic chest conditions should be avoided. A small number of elderly patients obstinately refuse operation. All these are best treated by some form of supporting pessary—a simple rubber ring if the shape of the vagina and the tone of the pelvic floor will retain it; otherwise a "cup and stem" if the patient herself can manage it. A few of the older, less active patients are comfortable with a simple supporting vulval pad covered by lubricant; a few can use a large vaginal sponge kept in position by a pad. All such patients must be carefully instructed in vaginal toilet, and sternly warned against neglect.

It will be noted that the operations of hysteropexy and ventrifixation designed to fix the uterus to the anterior abdominal wall have long ago passed out of good gynaecological practice. So, to a large extent, have the elaborate procedure of

Cultural examination, however, by determining the species of fungus, say, *M. felineum*, *T. gypsum* and *A. quinckeum*, can help to direct the attention to the primary source of infection, that is, cat, cattle or mouse respectively, and, in the case of *M. audouini* which is conveyed from child to child without any known intermediate host, to another infected child.

TREATMENT

The main methods of treatment can be divided into (a) physical removal of infected material, and (b) attempts at disinfecting the tissue.

(a) In the case of *onychomycoses*, owing to the impenetrable nature of the nail substance, antimycotics are of no avail and therefore more radical methods, such as avulsion of the nail, are indicated. When this procedure is adopted attempts to disinfect the nail beds should be proceeded with immediately so as to avoid re-infection which, however, often recurs despite assiduous care. In the case of infections of toenails it is occasionally necessary to resort to permanent excision of the nail and matrix owing to the tendency to re-infection.

Ringworm of the scalp, when due to *M. audouini*, is best treated by removal of the hair, and the methods available are epilation by X-rays or the internal administration of thallium acetate. The former should only be done by experienced radiologists, for the technique must be carried out accurately and the dosages measured very carefully for fear of producing areas of permanent alopecia. Thallium acetate has been used abroad with, so we are told, very satisfactory results, but once again this must be carried out with great care for fear of producing severe toxic reactions. The dosage of this substance is usually in the region of 8.5 mgm. per kgm. body weight, but varies with age and should be reduced in children approaching puberty. Further, it should not be overlooked that *M. audouini* infections of the scalp tend to clear up spontaneously at puberty. Cat ringworm of the scalp which, as previously mentioned, can be ascertained by cultural examination, usually responds to local measures, for fortunately it is a species of fungus which produces an appreciable tissue reaction and, if this can be increased by the application of irritant substances such as chrysarobin (derobin, dithranol) ointment, a cure can usually be effected without resorting to X-ray therapy. Keria of the scalp, by virtue of the severe tissue reaction produced, commonly result in spontaneous cure even without the aid of additional irritants.

One of the earliest antimycotics employed is, perhaps, iodine and this may be used in weak tinctures of 2 per cent. in *Tinea circinata*, provided it does not set up a dermatitis medicamentosa. Whitfield's ointment is of value, having the properties of both a mechanical remover in the form of salicylic acid, which is a keratolytic, and benzoic acid, which acts as the fungicide. This too is of value in the treatment of *Tinea cruris* and athlete's foot, but it is not as efficacious in the latter affection when the causal fungus is a trichophyton which produces vesicles and bullæ. Castellani's paint, which should always be used freshly made, is a highly effective fungicide, for it has the advantage of desiccating and desquamating the lesion besides its penetrating properties which enable it to reach the fungus. More recently phenylmercuric compounds have been introduced, but in my experience these often produce irritative changes as a result of sensitization to the compound, and should be used with caution. Salts of propionic acid and also, more recently, undecylenic acid, are becoming more popular and appear to act quite satisfactorily as fungicides without producing a dermatitis medicamentosa. It is probable that from higher fatty acids such as these further improvements in therapy may be expected.

dermatitis usually involves the dorsal aspect of the toes rather than the adjacent surfaces, and monilial infection gives rise to extensive sodden lesions between and beneath the toes.

Fungus infection of the scalp may produce a variety of lesions, the most common being discoid areas of short, broken, lustreless hairs, on a base exhibiting a varying degree of scaliness. When the patches are few in number the picture suggests infection with *M. audouini*, and numerous patches with a slightly greater degree of inflammatory reaction, infection with cat ringworm. This, however, is by no means a reliable rule, and as treatment of the latter may in many cases be conducted by employing more simple measures than those required for human ringworm, attempts should be made to determine the source of origin. Favus may produce the typical, saucer-like, yellow crusts with the characteristic musty odour, or broken hairs of irregular length, many occasionally even attaining full length. Keria of the scalp are similar to those already described on the hands, but are more frequently larger. Black-dot ringworm, manifested by the presence of scattered hair stumps broken off so closely to the surface of the scalp as to give the appearance of black dots, is due to the human types of the trichophyta, that is, the *T. endothrix* group, and can easily be overlooked.

Affections of the scalp sometimes confused with mycotic infections are alopecia areata and pseudo-pelade of Brocq. With regard to the former, the broken stumps of alopecia areata usually fall out readily, leaving a small bald area, but it should be stressed before leaving this subject that any bald patch present on a child's scalp should always be examined thoroughly to exclude the possibility of fungus infection. Pseudo-pelade of Brocq may resemble the end scar-leaving phase of favus, but the scars of the latter affection can usually be seen to be composed of isolated or coalescing, slightly depressed scars, each of about $\frac{1}{4}$ " to $\frac{3}{8}$ " in diameter.

Fungi are also capable of attacking the finger and toe nails, and invasion usually starts at the junction of the free and lateral margins of the nail, producing a discolouring, and at times thickening, of the nail plate which slowly leads to its destruction; but as the latter commonly involves the deeper layers of the nail substance, leaving a thin superficial veneer, the condition often remains undiagnosed until several nails are severely infected. The common differential diagnoses that must be excluded are psoriasis unguium and onychia secondary to paronychia. Psoriasis does not involve the nail plate in the way characteristic of fungus infection, i.e., from the antero-lateral margin towards the matrix, and further psoriatic affections of the nail fluctuate and may undergo spontaneous resolution. Onychia secondary to paronychia invariably starts with nail changes in the region of the lunule which pass distally with the growth of the nail.

Identification.—The presence of fungal elements in infections of the skin, hair or nails can be determined, after a little experience, by microscopical examination of preparations cleared in 7 per cent. to 25 per cent. potassium hydroxide. Wood's light is of considerable value in facilitating the rapid detection of fungus infection of hairs, but it should be borne in mind that only microspora fluoresce brightly, echorion less so, *Trichophyton ectothrix* poorly and at times fails to show, and *Trichophyton endothrix* never fluoresces. Satisfied that the infection is of fungal origin, the investigator may proceed by cultural methods to identify the species of fungus, for this may help him to decide on the most suitable method of treatment.

PREVENTION

Many attempts have been made, particularly in the United States, to prevent the spread of *Tinea pedis* in schools by insisting on the students passing through a trough of disinfecting fluid before congregating barefoot in gymnasia and dressing rooms, but the results are by no means as satisfactory as was at first anticipated.

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deprivation this can be relieved by sympathectomy, just as in other cases of vascular deprivation in which spasm is a predominant feature. White and Smithwick ("The Autonomic Nervous System", p. 229) conclude by saying that "It is therefore logical to recommend sympathectomy in patients with rheumatoid arthritis only if superimposed vasomotor and sudomotor disturbances are a cause of serious discomfort".

HEDLEY ATKINS, D.M., M.Ch., F.R.C.S.

Stellate Ganglion Block in Cerebral Thrombosis

QUERY.—Stellate ganglion blocks have been performed in America for the treatment of early cases of cerebral thrombosis. Is this procedure of any value, and what literature is there on the subject?

REPLY.—On the basis of Leriche's doctrine that a thrombus in an artery causes widespread spasm in the related arterial tree, the treatment of early cerebral arterial occlusion by novocain injection of the stellate ganglion on the side opposite the paralysis has theoretical value. Mackey and Scott (*Brit. med. J.*, 1938, *ii*, 1) reported 19 cases in which this procedure was carried out and concluded that it may be of value in a young person suffering from cerebral embolism, but that in the elderly patient with advanced arterial disease no beneficial results are obtained. The results are difficult to assess owing to varying rapidity of spontaneous recovery. A marked clinical improvement within a few minutes of the injection, and production of a Horner's syndrome, occurred only in their first case.

EDWARD TUCKWELL, F.R.C.S.

Intravenous Analgesia in Labour

QUERY.—There was recently an article in an Australian journal on intravenous injection of percaïne as an analgesic in labour, but no details of dosage, diluent or frequency were given. Has it been used in England to any extent, and what were the results?

REPLY.—A full account of "Intravenous Procaine for Obstetrical Anaesthesia" as used in the City Hospital, Welfare Island, New York, is given by Johnson and Gilbert in *Current Researches in Anaesthesia and Analgesia*, 1946, 25, 133. Only twenty cases are described and relief from pain was secured without mortality or serious accident. The authors emphasize the necessity of testing every case for procaine sensitiveness before treatment. In regard to "percaïne"—it is now always termed "nupercaine"—there is little information available of

its use in this country. The action of intravenous analgesic solutions in labour have not been sufficiently investigated to justify any routine use in general obstetric practice at the present time.

ARCHIBALD MARSTON, M.R.C.S., D.A.

Gold in the Treatment of Chronic Alcoholism

QUERY.—A patient of mine, who is a chronic alcoholic, tells me he wants to try what he calls the "gold" cure for chronic alcoholism. He is actually a dipsomaniac. Is there such a cure, and if so is it reputable and where could any details of it be obtained? I am told by the patient that there is a home specializing in this form of treatment somewhere near London. Perhaps you could also enlighten me on this point?

REPLY.—The "gold" treatment of alcoholics is one which had its day a number of years ago, and so far as I know it is not practised at all nowadays. There was an article in the *Lancet* in 1924 describing colloidal gold so given by injection. I have tried to find recent literature on the subject but without success and I know of no one who is practising the method. Nowadays we regard alcoholism as a symptom of nervous instability, and in addition to whatever treatment is given to break the habit we attempt to treat the underlying basic illness.

THOMAS TENNENT, M.D., F.R.C.P.

Palindromic Rheumatism

QUERY.—What is palindromic rheumatism, and what is its relationship, if any, to rheumatic fever? How is it treated?

REPLY.—Palindromic rheumatism is a term introduced by Hench and Rosenberg (*Arch. int. Med.*, 1944, 73, 293) to describe an "unusual, oft-recurring disease of joints and adjacent tissues" characterized by multiple afebrile attacks of acute arthritis and peri-arthritis, with pain, swelling, redness and disability, usually of one joint. The attacks, which as a rule develop suddenly, only persist for a few hours or days, and there is little constitutional disturbance. Parkes Weber (*Lancet*, 1946, *ii*, 931) has suggested extending the name to include cases of intermittent or recurrent hydrarthrosis and certain related conditions. The etiology is obscure, and, according to Hench and Rosenberg, it "is caused by some unknown irritant". It has no known relationship to rheumatic fever from which it can easily be distinguished in that the attacks are afebrile, short, and usually monarticular, and even after many years' duration there is never any evidence of cardiac involvement. Treatment is merely symptomatic during the attack, i.e. heat and analgesics.

NOTES AND QUERIES

Subscribers are invited to make use of the service provided in this section. Answers from experts will be obtained and dispatched as soon as possible to the senders of the queries. Publication of selected and suitable queries and replies is arranged according to available space.

Bee Stings

QUERY.—A patient who has started bee-keeping finds that her reaction to stings is disabling. What means exist for desensitization; what drugs can be used to alleviate the general symptoms, and what is the most efficacious line of treatment for the local lesion?

REPLY.—The problem of human reactions to bee stings is complex, and includes effects referable to (i) toxicity of the venom, (ii) allergy to bee protein, and (iii) rarely, allergy to pollen carried by the bee. Generally speaking, local reactions are predominantly due to the toxic action of the venom, and general reactions to allergy, although, of course, general toxic symptoms can occur, particularly when extensive stinging takes place. The development of tolerance to bee venom is believed to be due to an immunity reaction—although it is of interest that a state of "pathological immunity" has been reported in rheumatic individuals—and increased susceptibility to venom is probably an acquired sensitization, although its precise mechanism has not been clearly established. Allergic reactions are usually due to a specific hypersensitivity to bee protein, in contrast to decreased tolerance to the venom, which is not always strictly specific.

Treatment may be considered for (i) the local toxic effects, and (ii) the allergic reactions. Regarding the former, Pliny confessed he had no sure remedy for bee stings, and indeed the position to-day is not much better. Once the venom has been injected through the skin puncture, little can be done either to expel it or to neutralize it. After removal of the sting (which should be accomplished by gently scraping the skin and *not* by seizure with the thumb and forefinger, since the latter may result in more venom being injected from the poison sac which is usually left attached to the stinging mechanism), the application of ammonia or the blue-bag is the established routine. Regarding the treatment for allergic reactions, the general symptoms usually respond to 1:1000 solution of adrenaline, subcutaneously, although this is best given in small repeated doses, say, 0.1 to 0.2 c.cm. every thirty minutes. To ensure prompt treatment, it would probably be necessary to teach the patient to inject herself, in which case doses of 0.5 c.cm. of 1:5000 adrenaline would be easier for the patient to measure. Ephedrine, $\frac{1}{2}$ grain (32 mgm.) orally, is helpful, although the action is slower, but it may be quite satis-

factory for milder degrees of reaction. The new antihistamine drugs (benadryl, 50 mgm. capsule, antistin, 0.1 gm. tablet, and anthisan, 0.1 gm. tablet) might prove effective, and I would certainly recommend a trial.

The matter of prophylaxis by way of specific desensitization, although it has been found effective in selected cases, is not a simple routine treatment, and would entail preliminary skin testing of the patient with both venom and bee protein preparations (the latter are not available commercially), and a somewhat lengthy course of carefully graded desensitizing injections, which might not be easy in general practice. The best results, however, are obtained by specific avoidance, and in the present case this might be attempted by the adoption of suitable physical protective measures, and a trial of one of the new alkyl phthalate insect repellents, such as mylol.

DAVID HARLEY, M.D., F.R.I.C.

Sympathectomy in Rheumatoid Arthritis

QUERY.—Two patients with acute rheumatoid arthritis show evidence of grossly impaired peripheral circulation in the same extremities as are chiefly involved by the arthritis. In one case the affected part is the left ankle joint and foot, and the acrocyanosis is so severe as to suggest impending gangrene: in the other, there is a long-standing flexion deformity of both hands; the cold blue hands are not associated with thromboangiitis or cervical rib. In view of the known association of impairment of the circulation with rheumatoid arthritis, is there any indication for sympathectomy in cases of this kind? Is there any reason to hope that such treatment might have a beneficial effect on the arthritic process?

REPLY.—In 1927 Rowntree and Adson published their results on a series of cases of rheumatoid arthritis treated by sympathectomy (*J. Amer. med. Ass.*, 1927, 88, 694). Beneficial results were claimed, particularly in the younger patients, but no other surgeons have since confirmed these, and no further follow-up reports have come from the Mayo Clinic following the first enthusiasm for this measure. Dr. Walter Bauer recently treated five patients from the Massachusetts General Hospital by sympathectomy with no benefit so far as the arthritic condition was concerned. In many cases if the symptoms are predominantly due to vascular

received no sulphaguanidine: the death rate in the sulphaguanidine-treated group was 3.7 per cent., and in the control group 7.5 per cent. Sixty cholera patients were treated with sulphaguanidine in village homes, but no supportive saline treatment was possible; the death rate was 18.3 per cent. In a control home-treated series of 59 patients who did not receive sulphaguanidine the death rate was 40.7 per cent. In conclusion, the authors state that "sulphadiazine in the dosage used had no beneficial effect" but "sulphaguanidine is . . . of considerable value in the treatment of cholera".

Antistin in the Treatment of Chicken-Pox

L. GROSS (*Schweizerische Medizinische Wochenschrift*, February 21, 1948, 78, 159) reports the results obtained by the use of antistin during an outbreak of severe chicken-pox in 1947. Twenty of the children had active pulmonary tuberculosis: in 4 conservative treatment was employed, in 4 antistin in conjunction, and in 12 antistin was given from the beginning of the illness. The dosage used was:—in children up to three years of age, $\frac{1}{2}$ tablet morning and evening; in older children $\frac{1}{2}$ tablet twice or three times during the day and 1 tablet in the evening, and in infants $\frac{1}{2}$ tablet twice or thrice daily. The duration of treatment was on an average four to five days. The action of antistin was:—(1) prevention of itching and thereby improvement in the general condition and weight and prevention of secondary infection; (2) shortening of the course of the illness and a change in the character of the skin eruption in the form of quicker efflorescence and healing of the papules; (3) the course of the temperature curve was steeper and shorter, usually lasting for 2.8 days instead of 5.5 days in the untreated cases. No effect of the drug on the tuberculous affection was noted during an observation period of two months.

Combined Heparin-Dicoumarol Therapy in Myocardial Infarction

The results obtained in the treatment of twenty-five cases of myocardial infarction by combined heparin-dicoumarol therapy are recorded by H. I. Glueck, V. Strauss, J. S. Pearson, and J. McGuire (*American Heart Journal*, February 1948, 35, 269). The method adopted was as follows:—

After definite diagnosis had been established, and estimation of the initial prothrombin and clotting time carried out by the capillary tube method, unless the prothrombin time was prolonged and the patient in severe shock, dicoumarol, 200 mgm., was given orally, and simultaneously heparin, 300 mgm. added to a litre of 5 per cent. glucose in water, by continuous intravenous drip, starting at 20 drops per minute, and subsequently regulated in accordance with the measurement of the clotting time by the capillary tube method. Clotting time was deter-

mined at four-hourly intervals (except between midnight and 8 a.m.), and an attempt was made to maintain it between 8 to 10 minutes, the rate of the drip being increased or decreased accordingly. On an average the required rate was 20 to 25 drops per minute; some patients required 35 drops per minute. The prothrombin time was determined by the Quick method about twenty-four hours after the initial dose of dicoumarol, and thereafter daily until discontinuance of dicoumarol on the twenty-first day. Heparin administration was discontinued when the prothrombin level fell to 20 to 30 per cent. of normal concentration, usually between twenty-four and thirty-six hours after the first dose of dicoumarol. The average dose of heparin required during the period was 300 to 400 mgm. The importance of accurate laboratory determinations of the prothrombin concentration is emphasized; and dicoumarol was subsequently only administered after the daily prothrombin determination, the daily dosage varying from 0 to 250 mgm. if the prothrombin concentration was above 30 per cent. of normal, 100 to 200 mgm. dicoumarol were given, whereas if it was below 20 per cent. of normal, none was given. The total dosage used in the series ranged from 800 to 2,200 mgm. The period of treatment was twenty-one days.

In the series of twenty-five cases receiving combined heparin-dicoumarol therapy the death rate was 12 per cent., whereas in a control series not receiving anticoagulants the death rate was 32 per cent. Emboli occurred in six of the twenty-five control cases, and possibly in one of the heparin-dicoumarol treated series.

Thyroid Therapy in Hypogalactia

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Allergic Rhinitis

ALTHOUGH allergic rhinorrhœa is affected by endocrine factors, such as pregnancy and menstruation, and by climatic conditions, irritating fumes and chemicals, emotional factors, nasal obstruction and infection, the underlying causative factor is exposure to a substance to which the patient is sensitive (L. H. Crip: *Journal of the American Medical Association*, February 28, 1948, 136, 601). Sensitization tests—cutaneous, ophthalmic and nasal—sniff tests, and trial or

PRACTICAL NOTES

Cervical Cytology

THE importance of cytology in the early diagnosis of cervical cancer is stressed by J. E. Ayre (*Journal of the American Medical Association*, February 21, 1948, 136, 513), who advocates annual cytological testing as a means of increasing the percentage of surgical cures. Six methods are available:—(1) *the vaginal smear*, in which a negative reaction cannot be relied upon to eliminate the possibility of malignant uterine disease; (2) *the endocervical smear*, in the taking of which the cannula introduced into the cervical canal may bypass an early squamous cancer developing at the cervical portal; (3) *the endometrial smear* is not simple to obtain, and so is not recommended for routine use, but is strongly recommended as a secondary procedure when vaginal or cervical smears provide suspicious or indefinite endometrial cells; (4) *the smear from the cervical external os*, which gives the same all-over picture as the vaginal smear but possesses the advantage that a greater concentration of cervical squamous cells is collected for interpretation of cervical carcinoma of the common type; (5) *the selective scraping method*, which in the author's opinion is the method of choice for the identification of early microscopic squamous cancer of the cervix, as it is midway between an aspiration smear and a biopsy, and by scraping the circumference of the squamo-columnar junction of the cervix a true "surface biopsy" of these cells can be collected before their actual exfoliation; (6) *the cervical biopsy*, which is the most selective of all cytological methods, but in the presence of early cancer may miss a small microscopic growth. As regards the selective scraping method, it is recommended that a smear from the cervical external os should always be taken with the scraping in routine diagnostic practice, and in the presence of a large erosion the squamous epithelial margin must be scraped in its entire circumference under direct vision. The author concludes with the words "until a real cure for cancer is found, a yearly cytologic test offers the next best thing in diagnosis and control of uterine cancer".

Myanesin in Epilepsy

A REPORT of three cases in which intravenous administration of myanesin checked epileptiform attacks is given by A. R. Hunter and J. M. Waterfall (*Lancet*, March 6, 1948, i, 366). The first case was a man of seventy-two who was having almost continuous Jacksonian epileptic attacks affecting the right side of the body, but not the left; he had not lost consciousness. An

intravenous injection of myanesin, 0.4 gm., was given, and within thirty seconds the jerking ceased, the fits remaining in abeyance for nine minutes. The second case was a patient with encephalopathy who developed a series of epileptiform convulsions two hours after a lumbar encephalogram. The fits recurred every ten minutes and lasted for about five minutes. Myanesin, 0.5 gm., was given intravenously during the sixth fit, and within thirty seconds the patient became immobile and gradually recovered consciousness. No further convulsion occurred. The third case, a patient with subdural empyema, suffered recurrent epileptiform convulsions. He was given 10 c.cm. myanesin intravenously during an operation for his condition. The fits stopped and remained absent for about three hours, and on recurrence were stopped for a further two hours by administration of 0.5 gm. myanesin. Although the patient died on the third postoperative day, it was possible to keep him quiet during his illness by the use of intramuscular myanesin and occasional doses of paraldehyde. Myanesin was also used in a case of Parkinsonism about to undergo an operation for incarcerated hernia. Morphine and atropine premedication had no effect on the tremor, but after the patient had received 10 c.cm. myanesin the tremor had almost disappeared. It is stated that myanesin has relatively little effect on consciousness.

Sulphadiazine and Sulphaguanidine in Cholera

THE results obtained by the use of sulphadiazine and sulphaguanidine in the treatment of cholera are compared by C. L. Pasricha, B. M. Paul, A. C. Das Gupta, and A. K. Das (*Indian Medical Gazette*, September 1947, 82, 518). In a series of 425 patients with cholera to whom powdered sulphadiazine, in dosage of 1 gm. four-hourly, was given during the acute stage and then three times daily for two days, the death rate was 8.2 per cent.; in a control series of 423 patients who received no sulphadiazine the death rate was 9.5 per cent. All patients received the usual supportive saline treatment. In a second series, 451 patients received sulphadiazine in the above dosage, and 463 powdered sulphaguanidine in dosage of 3 gm. four-hourly during the acute stage, and then three times daily for two days. The death rates in this series were 7.9 per cent. in the sulphadiazine-treated cases, and 4.3 per cent. in the sulphaguanidine-treated cases. In a further series 1,118 hospitalized patients were given sulphaguanidine, and 1,170 were used as controls and

received no sulphaguanidine: the death rate in the sulphaguanidine-treated group was 3.7 per cent., and in the control group 7.5 per cent. Sixty cholera patients were treated with sulphaguanidine in village homes, but no supportive saline treatment was possible; the death rate was 18.3 per cent. In a control home-treated series of 59 patients who did not receive sulphaguanidine the death rate was 40.7 per cent. In conclusion, the authors state that "sulphadiazine in the dosage used had no beneficial effect" but "sulphaguanidine is . . . of considerable value in the treatment of cholera".

Antistin in the Treatment of Chicken-Pox

L. GROSS (*Schweizerische Medizinische Wochenschrift*, February 21, 1948, 78, 159) reports the results obtained by the use of antistin during an outbreak of severe chicken-pox in 1947. Twenty of the children had active pulmonary tuberculosis: in 4 conservative treatment was employed, in 4 antistin in conjunction, and in 12 antistin was given from the beginning of the illness. The dosage used was:—in children up to three years of age, $\frac{1}{2}$ tablet morning and evening; in older children $\frac{1}{2}$ tablet twice or three times during the day and 1 tablet in the evening, and in infants $\frac{1}{4}$ tablet twice or thrice daily. The duration of treatment was on an average four to five days. The action of antistin was:—(1) prevention of itching and thereby improvement in the general condition and weight and prevention of secondary infection; (2) shortening of the course of the illness and a change in the character of the skin eruption in the form of quicker efflorescence and healing of the papules; (3) the course of the temperature curve was steeper and shorter, usually lasting for 2.8 days instead of 5.5 days in the untreated cases. No effect of the drug on the tuberculous affection was noted during an observation period of two months.

Combined Heparin-Dicoumarol Therapy in Myocardial Infarction

THE results obtained in the treatment of twenty-five cases of myocardial infarction by combined heparin-dicoumarol therapy are recorded by H. I. Glueck, V. Strauss, J. S. Pearson, and J. McGuire (*American Heart Journal*, February 1948, 35, 269). The method adopted was as follows:—

After definite diagnosis had been established, and estimation of the initial prothrombin and clotting time carried out by the capillary tube method, unless the prothrombin time was prolonged and the patient in severe shock, dicoumarol, 200 mgm., was given orally, and simultaneously heparin, 300 mgm., added to a litre of 5 per cent. glucose in water, by continuous intravenous drip, starting at 20 drops per minute, and subsequently regulated in accordance with the measurement of the clotting time by the capillary tube method. Clotting time was deter-

mined at four-hourly intervals (except between midnight and 8 a.m.), and an attempt was made to maintain it between 8 to 10 minutes, the rate of the drip being increased or decreased accordingly. On an average the required rate was 20 to 25 drops per minute; some patients required 35 drops per minute. The prothrombin time was determined by the Quick method about twenty-four hours after the initial dose of dicoumarol, and thereafter daily until discontinuance of dicoumarol on the twenty-first day. Heparin administration was discontinued when the prothrombin level fell to 20 to 30 per cent. of normal concentration, usually between twenty-four and thirty-six hours after the first dose of dicoumarol. The average dose of heparin required during the period was 300 to 400 mgm. The importance of accurate laboratory determinations of the prothrombin concentration is emphasized; and dicoumarol was subsequently only administered after the daily prothrombin determination, the daily dosage varying from 0 to 250 mgm.; if the prothrombin concentration was above 30 per cent. of normal, 100 to 200 mgm. dicoumarol were given, whereas if it was below 20 per cent. of normal, none was given. The total dosage used in the series ranged from 800 to 2,200 mgm. The period of treatment was twenty-one days.

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elimination diets to determine if the causative factor be a food idiosyncrasy, should be carried out. (The ophthalmic test consists in instillation of a drop of the suspected material in the conjunctival sac; a positive reaction is manifested by local itching, congestion and lachrymation.) On the basis of the diagnosis, treatment is instituted, in the form of specific allergic therapy (avoidance and hyposensitization), medicinal measures, attention to nasal infection, and psychotherapy. The patient is instructed to occupy dust-free rooms and to use allergen-proof pillows; a diet is given in which foods to which the patient is sensitive are eliminated; hyposensitization is carried out with increasing doses of autogenous extract of house dust or other substance to which the patient is hypersensitive; irritating fumes and noxious occupational factors are avoided. Medicinal treatment is directed towards palliation, and includes the oral administration of ephedrine, 0.375 grain (24.4 mgm.) and phenobarbitone, 0.167 grain (10.8 mgm.), four-hourly when necessary. The antihistamine drugs are also useful—neoantergan, 50 mgm. four-hourly; benadryl, 25 to 50 mgm. four-hourly, or pyribenzamine, 25 to 50 mgm. four-hourly—but if side-effects such as drowsiness, palpitation, nausea and vomiting occur the drugs must be stopped. Local vasoconstrictors should be used but sparingly, as their continued use causes congestion and intensification of local symptoms. If nasal drops are prescribed the Proetz position should be employed. It is stated that rhinological treatment should always at first be conservative before institution of any surgical intervention. As emotional factors play a part in the etiology, psychotherapy may be of value.

Vitamin C and the Common Cold

THE value of vitamin C in the prevention of colds is reported by N. W. Markwell (*Medical Journal of Australia*, December 27, 1947, 34, 777), who has used the method in a considerable number of cases over a period of three years. The vitamin, in the form of ascorbic acid, must be administered immediately the first symptoms of a cold are felt, in dosage of $\frac{3}{4}$ gm., or more; the earlier the dose is given the more likely is it to be of value. If the cold has not been aborted in three to four hours another dose of ascorbic acid is taken, $\frac{1}{2}$ gm. or more, and if it should still persist on the second day 1 gm. is taken and repeated on the third day, the dose then being decreased. It is stated, however, that if the large dose of ascorbic acid is taken very soon after the onset of symptoms, the cold is aborted in the majority of cases. No ill-effects were noted; if more vitamin C than necessary is taken it appears to be excreted. In cases in which the

treatment fails to abort the cold it is stated that benefit is obtained from the vitamin C therapy, as reported by the author in cases of patients who previously suffered from repeated colds.

Treatment of Poliomyelitis with Fresh Convalescent Serum

THE use of fresh convalescent serum in the treatment of 117 cases of poliomyelitis is reported by H. Czickeli and R. Brauner (*Wiener Klinische Wochenschrift*, December 31, 1947, 59, 859). The serum was prepared as follows:—

At the end of the third or beginning of the fourth week of illness in older children and adults with the meningeal form of the disease, i.e., without paralysis, 200 to 400 c.cm. of blood was taken and coagulated by standing on ice for 24 to 36 hours. The serum was then centrifuged in order to free it of red blood corpuscles, and mixed to per cent. of its volume with 5 per cent. carbolic acid, so that an 0.5 per cent. carbolic acid-serum solution resulted (the carbolic acid destroys bacteria, but does not destroy the virus). The serum was next treated in a thermostat for 45 minutes at 56° to 58°, and put up in sterile penicillin bottles with rubber stoppers.

Of 117 patients treated with serum only one died and two developed paralysis; of 35 patients who did not receive any serum, 17 were already paralysed on admission, and of the 18 remaining patients one died and two became paralysed. Attention is drawn to the fact that in the epidemic of 1936 the mortality rate for 343 cases was 12.9 per cent., and 304 patients developed paralysis. In 1947 there were 152 cases between June and November of which only 23, less than 16 per cent. were paralysed, and the mortality rate was only 1.5 per cent.

Treatment of Psoriasis with Podophyllin

ACCORDING to A. Prassoli and R. Boveri (*Minerva Medica*, February 18, 1948, I, 191) the external application of podophyllin in psoriasis has many real advantages, e.g., ease of application, speedy disappearance of the plaques, absence of irritation. It induces remissions of variable duration, depending on the case and on the location of the disease: in some cases they are maintained as long as nine months. A solution of podophyllin 25 grains, alcohol 80 c.cm., and glycerin 20 c.cm. was painted on, and about $\frac{1}{2}$ cm. around, the plaques on alternate days. Treatment was continued until the scales fell from the periphery, when inflammation rapidly subsided. The centre remained pigmented, and a brown ring, 3-5 mm. wide, around the edge, may persist for some weeks. In some cases the podophyllin caused an eczematoid dermatitis but this reacted at once to cooling dressings. In some cases the podophyllin was increased to 35 per cent. without any reactions. There were no signs of intoxication. It is stressed that further investigations are necessary to evaluate long-term effects.

REVIEWS OF BOOKS

The Background of Therapeutics. By J. HAROLD BURN, M.D., F.R.S. London: Oxford University Press, 1948. Pp. vi and 367. Figures 58. Price 22s. 6d.

THE immense advances in therapeutics during the last ten years have made it difficult for the practising physician to keep abreast both with the scientific basis of new discoveries and with their practical application. Such gaps as may occur in our knowledge and teaching are amply filled by this book. Professor Burn has set out to consider in separate chapters most of the new therapeutic weapons which have been forged in recent years. The selection is wide and includes essays on thiouracil and obesity, on malaria and the steroid hormones, while the chapter on the process of disinfection is of importance to all engaged in the practice of medicine. Each chapter is a critical account of recent work with full references. The author addresses his work to "those engaged in teaching clinical medicine". It merits a much wider circulation, and any practitioner interested in treatment and in the underlying rationale in the use of the various powerful drugs he now commands will find much to interest, much to stimulate, and a great deal of everyday practical value in this attractive book.

Psychiatry: A Short Treatise. By WILLIAM A. O'CONNOR, L.M.S.S.A., D.P.M. Bristol: John Wright & Sons, Ltd., 1948. Pp. xi and 380. Price 35s.

THIS book is an exposition of the psychoses and psychoneuroses from the dynamic or psycho-biological viewpoint. Mental deficiency, forensic psychiatry, mental testing and statistical procedures in the study of the personality are not within its compass; but there is a short vivid chapter on the psychopathic personalities (the expressions "rhythmic evil-doer" and "ego-philiac" are instantly intriguing), and another, rather more diffuse, on psychosomatic disturbances in children. There is no bibliography, and although there are many dated historical acknowledgments to the work of individuals, there are no detailed references. A glossary and index are provided. The clinical syndromes—especially the psychoses—are clearly and simply described, and are illustrated by well-chosen concise clinical records. There is sound advice about case-taking, which is rightly kept on a factual level, and as free from technicalities as possible. The principles of treatment are briefly stated in each group of disorders, but technical methods are not described in much detail.

Especial weight is attached to Freudian principles. This is an easily read book, with a strongly individualistic flavour. It should be helpful to the beginner as an adjunct to more detailed and compendious works.

Sexual Behaviour in the Human Male. By ALFRED C. KINSEY, WARDELL B. POMEROY AND CLYDE E. MARTIN. Philadelphia and London: W. B. Saunders Co., 1948. Pp. xv and 804. Figures 173. Price 32s. 6d.

THIS volume, "presented as an objective factual study of sexual behaviour in the human male", is based upon a study of 12,000 persons who have contributed the requisite history of their sexual life. It is sponsored by the National Research Council's Committee for Research on Problems of Sex, financed by the Rockefeller Foundation, and written by a distinguished American zoologist. Of the thoroughness, care and objectivity with which it has been compiled there can be no doubt. As a contribution to the study of a difficult subject it can claim to be unique. All the data were obtained through first-hand interviews, which so far have been limited to individuals resident in the United States. For all who are interested in the problem, whether physicians, psychiatrists, lawyers or welfare officers, this compendium will prove indispensable. To assess its true significance is not possible within the limits of a short review, but it can certainly be described as thought-provoking.

Sex Fulfilment in Married Women. By HELENA WRIGHT, M.B., B.S. London: Williams and Norgate Ltd., 1947. Pp. 96. Price 5s.

IN making her assertion that not more than 50 per cent. of married women obtain sexual satisfaction Dr. Wright concludes that this is not entirely due, as was previously thought, to ignorance of the technique of the art of love. Her new book will prove an extremely practical help to the bride discouraged by finding that complete spiritual and physical union are not automatic concomitants of marriage. The more experienced married woman, driven perforce to a state of despondency or resignation and unaware of her potentialities, will derive no less benefit and encouragement from its pages. Once more some of the cobwebs of tradition which surround the sex relationship have been swept away; this book should be read by all who may be brought into consultation on its problems.

Emotional Problems of Living. By O. SPURGEON ENGLISH, M.D., and GERALD H. J. PEARSON, M.D. London: George Allen & Unwin, 1947. Pp. 438. Price 16s.

THIS book is the work of two teachers of psychiatry at Temple University, Philadelphia. It attempts the important and difficult task of tracing personality development from the infant to the adult and of showing how emotional conflicts arise which result in neurosis. Some ninety authorities are quoted in the text. Psycho-analytical concepts are used throughout. The text abounds in clinical records of children and adults, and advice regarding treatment is eminently practical, other methods than those of Freud being described, particularly those used at the Phipps Clinic. This book should greatly help in the understanding and treatment of neurotic illness, even though some of the more obscure Freudian psychopathology will appear unconvincing.

The Personality of the Pre-School Child.

By WERNER WOLFF, Ph.D. London: Wm. Heinemann (Medical Books) Ltd. Pp. xvi and 341. Price 25s.

THIS is essentially a book for the serious student of child psychology. Dr. Wolff makes a contribution to the study of personality similar to that made by Gesell regarding the child's developing abilities. He combines the methods of observation and controlled experiment, giving a balanced viewpoint. His "depth psychology" takes us further than the pure observational methods of the behaviourists and also avoids the pitfalls of those psychoanalysts who make theoretical deductions based on the study of relatively small numbers of children. The author stresses the difference in the mental structure of the child and adult, thus avoiding the misleading findings of those who view the child simply as a "small adult". The child's "search for himself" is seen as the unifying concept behind all aspects of the pre-school child's behaviour.

Detoxication Mechanisms: The Metabolism of Drugs and Allied Organic Compounds.

By R. TECWYN WILLIAMS, Ph.D., D.Sc. London: Chapman & Hall Ltd., 1947. Pp. viii and 288. Price 25s.

DR. WILLIAMS is to be congratulated on compressing into some 221 pages practically all that is known of the metabolism of synthetic organic compounds in mammals. The introductory chapter summarizes the development of the study of this subject and enumerates the nine biochemical detoxication mechanisms. The

average medical man will no doubt find the terse chemical literature hard going, but he cannot fail to be impressed by the amount of information available. It is to be regretted that no account of the metabolism of certain organic compounds which occur naturally and have been synthesized, to wit vitamins, oestrogens and androgens, has been included. The final chapter, which deals with theoretical considerations and conclusions, is a disappointment. The general format of the book is good and the index and bibliography are a matter for congratulation.

Paravertebral Block: Minor Sympathetic Surgery. By FELIX MANDL, M.D., F.I.C.S. London: Wm. Heinemann (Medical Books) Ltd., 1948. Pp. xvii and 330. Figures 20. Price 32s.

THE author writes this book with over twenty years' experience of the subject; he describes his failures and his successes with equal detail and, after reviewing the results of other authorities, gives his own opinions. The relief of pain, especially cardiac pain, is discussed at length and the various disorders of the extremities in which sympathetic interruption has been tried are listed and critically reviewed. For all who are interested in the surgery of the autonomic nervous system and the subject of visceral pain this book offers both encouragement and sound advice. There is a very complete bibliography and numerous case reports on each section of the book.

Chronic Ill-Health: Relieved by Drainage of the Para-nasal Sinuses. By ROSA FORD, M.B., D.O. London: Henry Kimpton, 1948. Pp. xii and 104. Figures 13. Price 6s.

THE author of this small book combines the rôles of enthusiast and a voice crying in the wilderness. Such people are not always wrong in their contentions, but are apt to stress a detail and make of it the main theme of their subject-matter. Few physicians or oto-laryngologists would deny that chronic nasal sinusitis may be the focus for ill-health elsewhere in the body, and all would agree that this disease may be overlooked; but few would agree that "the primary focus of chronic infection is always in the sinuses". Yet this basic claim is made in the preface. A great deal of the book is taken up with descriptions of patients suffering from a variety of maladies from eye diseases to leucorrhœa, from duodenal ulcer to disseminated sclerosis—and from supposed concomitant chronic sinusitis. The chapters on etiology and pathology carry little conviction, and those on

the diagnosis and treatment of sinusitis even less. The remarkable suggestion is made that all patients showing a contraction of the visual fields must needs be suffering from sinus disease; the perimeter thus becomes the instrument of choice in diagnosing a rhinological condition. Under treatment we find a mixture of the orthodox (in the form of steam inhalations and operations) with the bizarre. One drop of a mixture of glycerin and normal saline instilled into the nostril is "astonishingly effective in stimulating secretion". Again, if that does not work, pledgets soaked in hydrogen peroxide are inserted into the nostrils and, as might be expected, these usually produce a gratifying nasal discharge. Aloe is given internally because it gives "an impetus to expulsion" of the secretions from the sinuses.

Medizinische Terminologie. BY RUDOLF ABDERHALDEN, M.D. Basle: Benno Schwabe & Co., 1948. Pp. 1213. Price Sw. frs. 32.

THIS book on medical, scientific and chemical terminology is splendidly compiled. The author takes the accepted terminology, in German, Latin or in English, or *vice versa*, and then provides each with a lucid explanation in German. Not only will those reading German medical literature find it of great value—it is a valuable aid for the translator.

NEW EDITIONS

GARDINER'S *Handbook of Skin Diseases*, revised by John Kinnear, O.B.E., M.D., M.R.C.P., D.L., in its fifth edition (E. & S. Livingstone Ltd., 15s.) has been brought up to date in all sections. Among the new additions are the use of BAL in exfoliative dermatitis, benadryl in the control of urticaria, DDT in pediculosis, calciferol in lupus vulgaris, and penicillin in impetigo and staphylococcal and streptococcal skin infections.

The Science and Practice of Surgery, by W. H. C. Romanis, M.Ch., F.R.C.S., F.R.S., and Philip H. Mitchiner, C.B., C.B.E., M.D., M.S., F.R.C.S., D.Ch., in its eighth edition (J. & A. Churchill Ltd., Vol. I and II, 25s. each) has been extensively revised. Two new chapters, on plastic surgery and radiotherapy, have been included in Vol. I, and there is a useful section devoted to chemotherapy. Both volumes, one of which deals with general surgery and the other with regional surgery, are richly illustrated.

Textbook of General Surgery, by Warren H. Cole, M.D., F.A.C.S., and Robert Elman, M.D., F.A.C.S., in its fifth edition (D. Appleton-Century Company, \$11.00) has been extensively revised in the light of the many advances in surgery

during the war years. There is a section on chemotherapy, with a subsection on streptomycin; a chapter devoted to different forms of anaesthesia; new methods for treating burns and fractures—these are but a few of the many advances incorporated in the new edition, which is beautifully produced and illustrated, containing in all 558 figures.

A Manual of Pharmacology, and Its Applications to Therapeutics and Toxicology, by Torald Sollman, M.D., in its seventh edition (W. B. Saunders Co. Ltd., 57s. 6d.) is so full of new material that it is possible to mention only a few of the additions—the antihistamine drugs, anticonvulsants, folic acid, BAL, vitamins, hormones and the antibiotics. This work is unique in that as well as discussing the chemical formulæ, origin and modes of action of the different drugs, their absorption, excretion, toxic actions and therapeutic uses are explained.

Milk Products, by Wm. CLUNIE Harvey, M.D., D.P.H., and Harry Hill, F.R.San.I., A.M.I.S.E., F.I.S.A., in its second edition (H. K. Lewis & Co. Ltd., 30s.) has been brought up to date to include new legislation and advances in the control and production of milk. There is an illuminating section on dried milk, and the chapter on subsidiary uses for milk will be read with interest. The new edition is well illustrated, and shows by the new apparatus exhibited how the industry has advanced in methods of control.

THE second edition of the *Natural History of Disease*, by JOHN A. RYLE, M.D., F.R.C.P. (Oxford University Press, 22s. 6d.) follows its predecessor after a long interval, and consequently much revision has been undertaken. The author in the preface again stresses the importance of knowledge of the natural history of disease and the value of such knowledge in prognosis.

Aids to Gynaecology, by W. R. Winterton, M.B., B.Ch., F.R.C.S., M.R.C.O.G., in its tenth edition (Ballière, Tindall and Cox, 5s.) contains a new chapter on gynaecological endocrinology. The many advances in chemotherapy since the publication of the previous edition in 1939 are also among the new additions.

Pathological Histology, by Robertson F. Ogilvie, M.D., F.R.C.P.Ed., F.R.S.E., in its third edition (E. & S. Livingstone Ltd., 37s. 6d.) has been extensively rewritten and new material added. The coloured photomicrographs, which total 260, and show not only the morphology of the lesions but the staining reactions of the tissues and pigmentary changes, are a distinctive feature of this work.

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Detoxication Mechanisms: The Metabolism of Drugs and Allied Organic Compounds.

By R. TECWYN WILLIAMS, Ph.D., D.Sc. London: Chapman & Hall Ltd., 1947. Pp. viii and 288. Price 25s.

DR. WILLIAMS is to be congratulated on compressing into some 221 pages practically all that is known of the metabolism of synthetic organic compounds in mammals. The introductory chapter summarizes the development of the study of this subject and enumerates the nine biochemical detoxication mechanisms. The

average medical man will no doubt find the terse chemical literature hard going, but it cannot fail to be impressed by the amount of information available. It is to be regretted that no account of the metabolism of certain organic compounds which occur naturally and have been synthesized, to wit vitamins, oestrogen and androgens, has been included. The final chapter, which deals with theoretical considerations and conclusions, is a disappointment. The general format of the book is good and the index and bibliography are a matter for congratulation.

Paravertebral Block: Minor Sympathetic Surgery. By FELIX MANDL, M.D., F.I.C.S. London: Wm. Heinemann (Medical Books) Ltd., 1948. Pp. xvii and 330. Figures 20. Price 32s.

THE author writes this book with over twenty years' experience of the subject; he describes his failures and his successes with equal detail and, after reviewing the results of other authorities, gives his own opinions. The relief of pain, especially cardiac pain, is discussed at length and the various disorders of the extremities in which sympathetic interruption has been tried are listed and critically reviewed. For all who are interested in the surgery of the autonomic nervous system and the subject of visceral pain this book offers both encouragement and sound advice. There is a very complete bibliography and numerous case reports on each section of the book.

Chronic Ill-Health: Relieved by Drainage of the Para-nasal Sinuses. By ROSA FORD, M.B., D.O. London: Henry Kimpton, 1948. Pp. xii and 104. Figures 13. Price 6s.

THE author of this small book combines the rôle of enthusiast and a voice crying in the wilderness. Such people are not always wrong in their contentions, but are apt to stress a detail and make of it the main theme of their subject-matter. Few physicians or oto-laryngologists would deny that chronic nasal sinusitis may be the focus for ill-health elsewhere in the body, and all would agree that this disease may be overlooked; but few would agree that "the primary focus of chronic infection is always in the sinuses". Yet this basic claim is made in the preface. A great deal of the book is taken up with descriptions of patients suffering from a variety of maladies from eye diseases to leucorrhœa, from duodenal ulcer to disseminated sclerosis—and from supposed concomitant chronic sinusitis. The chapters on etiology and pathology carry little conviction, and those on

the diagnosis and treatment of sinusitis even less. The remarkable suggestion is made that all patients showing a contraction of the visual fields must needs be suffering from sinus disease; the perimeter thus becomes the instrument of choice in diagnosing a rhinological condition. Under treatment we find a mixture of the orthodox (in the form of steam inhalations and operations) with the bizarre. One drop of a mixture of glycerin and normal saline instilled into the nostril is "astonishingly effective in stimulating secretion". Again, if that does not work, pledgets soaked in hydrogen peroxide are inserted into the nostrils and, as might be expected, these usually produce a gratifying nasal discharge. Aloes is given internally because it gives "an impetus to expulsion" of the secretions from the sinuses.

Medizinische Terminologie. BY RUDOLF ABDERHALDEN, M.D. Basle: Benno Schwabe & Co., 1948. Pp. 1213. Price Sw. frs. 32.

THIS book on medical, scientific and chemical terminology is splendidly compiled. The author takes the accepted terminology, in German, Latin or in English, or *vice versa*, and then provides each with a lucid explanation in German. Not only will those reading German medical literature find it of great value—it is a valuable aid for the translator.

NEW EDITIONS

GARDNER'S *Handbook of Skin Diseases*, revised by John Kinnear, O.B.E., M.D., M.R.C.P., D.L., in its fifth edition (E. & S. Livingstone Ltd., 195.) has been brought up to date in all sections. Among the new additions are the use of BAL in exfoliative dermatitis, benadryl in the control of urticaria, DDT in pediculosis, calciferol in lupus vulgaris, and penicillin in impetigo and staphylococcal and streptococcal skin infections.

The Science and Practice of Surgery, by W. H. C. Romanis, M.Ch., F.R.C.S., F.R.S., and Philip H. Mitchiner, C.B., C.B.E., M.D., M.S., F.R.C.S., D.Ch., in its eighth edition (J. & A. Churchill Ltd., Vol. I and II, 25s. each) has been extensively revised. Two new chapters, on plastic surgery and radiotherapy, have been included in Vol. I, and there is a useful section devoted to chemotherapy. Both volumes, one of which deals with general surgery and the other with regional surgery, are richly illustrated.

Textbook of General Surgery, by Warren H. Cole, M.D., F.A.C.S., and Robert Elman, M.D., F.A.C.S., in its fifth edition (D. Appleton-Century Company, \$11.00) has been extensively revised in the light of the many advances in surgery

during the war years. There is a section on chemotherapy, with a subsection on streptomycin; a chapter devoted to different forms of anaesthesia; new methods for treating burns and fractures—these are but a few of the many advances incorporated in the new edition, which is beautifully produced and illustrated, containing in all 558 figures.

A Manual of Pharmacology, and Its Applications to Therapeutics and Toxicology, by Torald Sollman, M.D., in its seventh edition (W. B. Saunders Co. Ltd., 57s. 6d.) is so full of new material that it is possible to mention only a few of the additions—the antihistamine drugs, anticonvulsants, folic acid, BAL, vitamins, hormones and the antibiotics. This work is unique in that as well as discussing the chemical formulæ, origin and modes of action of the different drugs, their absorption, excretion, toxic actions and therapeutic uses are explained.

Milk Products, by Wm. CLUNIE Harvey, M.D., D.P.H., and Harry Hill, F.R.San.I., A.M.I.S.E., F.I.S.A., in its second edition (H. K. Lewis & Co. Ltd., 30s.) has been brought up to date to include new legislation and advances in the control and production of milk. There is an illuminating section on dried milk, and the chapter on subsidiary uses for milk will be read with interest. The new edition is well illustrated, and shows by the new apparatus exhibited how the industry has advanced in methods of control.

THE second edition of the *Natural History of Disease*, by JOHN A. RYLE, M.D., F.R.C.P. (Oxford University Press, 22s. 6d.) follows its predecessor after a long interval, and consequently much revision has been undertaken. The author in the preface again stresses the importance of knowledge of the natural history of disease and the value of such knowledge in prognosis.

Aids to Gynaecology, by W. R. Winterton, M.B., B.Ch., F.R.C.S., M.R.C.O.G., in its tenth edition (Ballière, Tindall and Cox, 5s.) contains a new chapter on gynaecological endocrinology. The many advances in chemotherapy since the publication of the previous edition in 1939 are also among the new additions.

Pathological Histology, by Robertson F. Ogilvie, M.D., F.R.C.P.Ed., F.R.S.E., in its third edition (E. & S. Livingstone Ltd., 37s. 6d.) has been extensively rewritten and new material added. The coloured photomicrographs, which total 260, and show not only the morphology of the lesions but the staining reactions of the tissues and pigmentary changes, are a distinctive feature of this work.

NOTES AND PREPARATIONS

Royal Medical Benevolent Fund

A LETTER from the Chairman of the Royal Medical Benevolent Fund, Mr. R. M. Handfield-Jones, M.C., M.S., F.R.C.S., announces the opening of, and gives a progress report on, Westmoreland Lodge, the first home to be opened by the Fund. Westmoreland Lodge accommodates a number of old ladies, each of whom has her own bed-sitting room. A quotation from the Chairman's letter indicates the appreciation of these beneficiaries:—

"I do like opening the front door of this house because I know I am coming in to such a happy atmosphere". . . the success of Westmoreland Lodge leads us on to other thoughts. Might we not think of a similar house for men, and should we also provide for the sick and bed-ridden? To a certain extent the answers to these questions depend upon the reaction of the profession to our work".

The address of the Royal Medical Benevolent Fund is, 1 Balliol House, Manor Fields, Putney, London, S.W.15.

EMPIRE RHEUMATISM COUNCIL

THE Eleventh Annual Report of the Empire Rheumatism Council, covering 1947, is a record of steady progress. The investigation into the causation of rheumatoid arthritis has been maintained, and a research worker has been appointed to study the allergic aspects of rheumatism. This year also saw the re-opening of the Council's laboratory at the Hospital of St. John and St. Elizabeth. Although many new methods of treatment have been submitted to the Council, nothing of note has emerged during the year. The Ministry of Food Advisory Committee has agreed to a recommendation of the Council's Scientific Advisory Committee that extra milk should be made available for cases of active rheumatoid arthritis. It is pointed out that the coming into force of the National Health Act will not affect the need of the Council for funds with which to prosecute research.

NATIONAL ASSOCIATION FOR THE PREVENTION OF TUBERCULOSIS

IN conjunction with the Joint Tuberculosis Council the following refresher courses are being organized during 1948:—

Radiology in Connexion with Tuberculosis and Chest Diseases, at Leeds from September 20 to 23.

Non-Pulmonary Tuberculosis, including Lupus, at Lord Mayor Treloar Hospital, Alton, from October 5 to 7.

Clinical Courses at Cheshire Joint Sanatorium, Market Drayton, Salop, May 11—13; May 25—27.

The Social Aspect of Tuberculosis and Chest Diseases, at Leeds from September 23 to 24.

Full details of these courses, the last of which is intended for nurses, health visitors, almoners and chief administrators, may be obtained from N.A.P.T., Tavistock House North, London, W.C.1.

PUBLICATIONS

Pediatrics, the journal of the American Academy of Pediatrics, Inc., is a new monthly journal devoted to child health and welfare. Published in America by Charles C Thomas, it is obtainable in Great Britain from Blackwell Scientific Publications, Ltd., 48 Broad Street, Oxford. Annual subscription 63s. per annum.

Basic Facts of Health Education (the Pharmaceutical Press, 7s. 6d.) is a selection of articles from the Ministry of Health Bulletin which have appeared in the *Pharmaceutical Journal*, 1944-47. Compiled in book form, it is readily available for reference.

The Foundations of Health in Childhood, Norman B. Capon, M.D., F.R.C.P., Professor of Child Health, University of Liverpool, is a Convocation lecture, 1947, of the National Children's Home, and deals, among other subjects, with the nutrition, hygiene, and attainment of optimum health for children. Published by the National Children's Home Orphanage, Highbury Park, London, N.5, price 2s. 6d.

Tuberculosis in the Commonwealth, 1947 (National Health Service, 15s.), is the complete transactions of the Commonwealth and Empire Health and Tuberculosis Conference, 1947. Among the many subjects covered are the National Health Service Act, in relation to tuberculosis, sanatorium design, Colonial tuberculosis services, and specific treatment.

Home Ambulance Service is the annual report of a register of ambulance stations in England, Wales, the Channel Islands and the Isle of Man. It is published by the Order of St. John and the British Red Cross Society.

OFFICIAL PUBLICATIONS

Memorandum on Vaccination Against Smallpox (Memo. 312/Med.) deals with the subjects of primary vaccination of infants, school children, adolescents and adults, and also re-vaccination of children and adults. The pamphlet, which is illustrated, is published by H.M. Stationery Office, price 2d.

Public Health (Aircraft) Regulations, 1948 (C. 28/48); *Health Control at Airports* (Mem. 50) are the new health rules for air travel issued by the Ministry of Health. Copies are obtainable from H.M. Stationery Office, price 5d. and 6d. respectively.

The contents of the June issue, which will include a symposium on "Aviation Medicine", will be found on page lxx at the end of the Advertisement Section.



THE PRACTITIONER

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AVIATION MEDICINE

INTRODUCTION

By THE RT. HON. LORD NATHAN OF CHURT, T.D., D.L.

Minister of Civil Aviation.

It cannot be stressed too strongly or too frequently that in civil aviation the principle of ensuring the maximum safety in flight must govern all our activities. Our success must depend, of course, upon the efforts not of any one individual but of a team in which we all can play our full part. It is in connexion with the human factor in flying that medicine plays its most important rôle as a member of the team, and there are few, if any, other commercial activities in which medicine takes such a responsible part as in civil flying.

In flying, the human factor must always be kept in proper perspective. It is upon the fitness—in the widest sense—of the crews that the safety of the passengers largely depends. Especially in the development of new types of aircraft, and of new types of aircraft equipment, must the capacity of man, his fitness for his task, always be kept in mind. The aircraft and its equipment have to be designed to fit man—the design of man cannot be altered to fit the machine.

The study of the human factor in flying has been carried on for many years, not only in this country, although our contributions have been very considerable, but in other countries as well. The problems of Service flying and Service flying crews have hitherto, owing to the world situation, overshadowed those of civil flying and civil flying crews; but now, with the expansion and development of our civil aviation fleets, we are likely to encounter more and more problems peculiar to civil flying. Although the research work in aviation medicine has in the past been designed mainly to meet Service needs—only a small proportion has been directed specifically to problems peculiar to civil flying—this does not mean that we, in civil aviation, have not benefited from it. The human problems of work in the air are to a great extent problems common to both Service and civil air-

crews, and a high proportion of the results of research work can be, and is, applied in civil flying. In our research work into aviation medicine problems in civil flying we shall continue in the future, as in the past, to be associated with the parallel work in Service flying.

The selection of the right type of person for training as a crew member is of the utmost importance. First, all candidates must undergo a general medical examination to ensure their physical fitness for their duties in the air. Having once taken up civil flying as a career they are subjected to further medical examination, both periodically and after major incidents in their medical history. Thus, right throughout their flying career they are kept under medical supervision. But our efforts do not end there. Our aim is to remove all obstacles to full human efficiency during flight and throughout each airman's flying career. Some of these obstacles the airmen can themselves overcome if they are given proper advice. Others can be removed, or at least their effect reduced, by improved design.

Loss of efficiency during flight is caused by the onset of fatigue. Aviation medicine researches have already enabled us to do a great deal towards avoiding or delaying the onset of fatigue by improving the design of the aircraft, its equipment and special devices worn by the crews. For example, it is obviously important that pilots' controls should be placed in the most favourable positions and that seats should be made as comfortable as possible. A great deal has already been done towards that end. Furthermore, instrument dials have been simplified to make them easier to read quickly and accurately, instruments have been re-grouped, microphones and ear-phones have been improved in design.

But in civil and commercial flying we have not only to think of and plan for the comfort of the crews. We must also have our eyes on the comfort and well-being of our passengers. Much has already been accomplished. But we look to our medical friends for further advice and assistance on questions of vibration, oxygen equipment, control of pressurization, diet, and many other important matters.

We have by no means found all the answers yet to the problems which already beset us; and with the rapid development of aircraft, new and more difficult problems are arising. Medicine will continue to have a great part to play in our flying activities.

SOME PHYSIOLOGICAL HAZARDS OF FLYING

By W. RANDOLPH LOVELACE, II., M.D., M.S., F.A.C.S., F.I.C.S.

Head of a Section on Surgery, Lovelace Clinic; Medical Director of Trans-World Air Lines

AND CLAYTON S. WHITE, M.D.

Head of Aviation Medical Section, Lovelace Clinic, Albuquerque, New Mexico, U.S.A.

THOSE concerned with aviation have paid increasing attention to the effects of decreased barometric pressure on man, especially since the last war. The physiological aspects of flight are fundamentally the same, although considerable quantitative difference in the physiological hazards of flying exists between military and commercial aviation. The service flight surgeon has a difficult task both in research and in the practice of aviation medicine. Superficially, it might appear that the private practitioner plays a part in civil aviation which is slight by comparison. This is not true. In aviation, the civilian doctor has two primary obligations to the public: the physical examination and medical maintenance of the flying personnel of commercial aviation, and the air-passenger population. Since the practitioner meets the medical problems of the public, it is essential he be versed in the basic principles of aviation medicine. Even though some may be authorities on aviation physiology, often it will be necessary to base an opinion upon considered judgment rather than upon material in the literature.

The information and bibliography which follow, have been chosen primarily to aid the family doctor in an appraisal of physiological fitness for air travel, and to stimulate aero-medical research in the fields of pathophysiology, pædiatrics, and geriatrics. The physiological hazards of flying are related to (1) decrease in the partial pressure of oxygen with increase of altitude; (2) changes in volume or pressure of gases with variation in altitude; (3) temperature changes; (4) motion; (5) toxic gases; (6) noise and vibration; (7) survival; (8) psychiatric factors.

ALTITUDE AND OXYGEN PRESSURE

Unpressurized aircraft seldom operate at a pressure altitude exceeding 15,000 or 16,000 feet. The bulk of flying is done between 2000 and 10,000 feet, although in some mountainous areas flying at 11,000 to 14,000 feet is routine. Pressurized planes in current use operate up to 25,000 feet with a cabin altitude of 8000 to 10,000 feet. This year, however, pressurized aircraft capable of flying to 30,000 feet with a cabin altitude from 8000 to 10,000 feet will be in use by airlines flying world-wide schedules.

CHANGES RELATED TO DECREASE IN PARTIAL PRESSURE OF OXYGEN

Table 1 (Best and Taylor, 1940) summarizes the accepted values for partial pressures of oxygen in the inspired and alveolar air, the arterial and

venous blood, and the tissues, for "normal" resting man at sea level. The pressure gradient, inspired air-to-tissue, may be roughly thought of as the basic essential pressure-head which drives oxygen towards the individual tissue cell.

In table 2 are data showing the changes in barometric pressure at increasing pressure altitudes, along with the decrease in the partial pressures of oxygen, the percentage oxygen saturations of the blood, and the amount of functional disturbance to be anticipated in young, healthy, unacclimatized

TABLE 1.

Oxygen Exchange Inspired Air to Tissue due to Differences in Partial Pressure of Oxygen. Figures are those under Sea Level Conditions, from Best and Taylor (1940).

Partial Pressure of Oxygen in Millimeters of Mercury				
Air Oxygen	Alveolar (lung) Oxygen	Blood in Lungs	Blood in Tissues	Tissues
158.25	101.2	<div style="border: 1px solid black; padding: 10px; text-align: center;"> <p>Arterial Blood</p> <p>100 —————→</p> <div style="border: 1px solid black; padding: 5px; margin: 5px auto; width: 80%;"> <p>Venous Blood</p> <p>←———— 40</p> </div> </div>		10 to 20 (mean-estimated)

adults at rest or doing light work (Boothby, 1944; Hensen, *et al.*, 1947; Halstead, *et al.*, 1944; Matthews, 1945; Baxter, *et al.*, 1944). Failure of judgment and euphoria commonly occur early in hypoxia without the average individual's realization. It is also well to know that convulsive seizures and mania have been observed in apparently healthy young males at altitudes as low as 15,000 to 18,000 feet (White, 1943-47).

Matthews (1945), Armstrong (1939), Symonds (1943), Fulton (1941), and the physicians and physiologists in the U.S. Army Air Forces (AAF Manual, 1945) have ably summarized the effects of oxygen lack as seen in relatively young healthy individuals. There is a pressing need, however, for more data which will be applicable to the unselected flying passenger public. Matthews (1945), for instance, speaking of the effects of oxygen lack, states that there are "three primary factors determining the intensity of symptoms: (1) the oxygen partial pressure of exposure; (2) the duration of exposure, and (3) the muscular activity of the subject". At least two other factors need to be considered when thinking about airline passengers; namely, (4) variations in the physiological state of an individual from time to time, and (5) the patho-physiological condition of a person as determined

by age, illness, or predisposing factors to disease.

Gray (1944, 1945), Fenn, Rahn and Otis (1946), and Otis, Rahn, Epstein, and Fenn (1946) have pointed out the complex considerations necessary to arrive at an accurate expression of alveolar air in terms of altitude. They elucidate the existence of a physiological "unsteady state", during which dynamic changes affecting the performance of an individual at altitude occur. The main contribution made to the present problem is to (1) help to elucidate the wide "normal" variations in the tension of oxygen in the alveolar air and in the arterial blood reported in table 2; (2) urge conservatism in the interpretation of data in the literature reported as "average" or "normal" figures; and (3) emphasize the factor of time during which the physiological state changes due to variations in the respiratory quotient, ventilation rate, carbon dioxide, and oxygen concentrations in the blood.

In considering the patho-physiological variations present in many airline passengers it is instructive to note that Houston (1946), among others, has shown that the oxygen saturation of the arterial blood is extremely sensitive to small changes in pulmonary ventilation which are practically unnoticeable subjectively, and that an increase in arterial oxygen saturation of from 10 to 20 per cent. may follow an increase in ventilation to double

TABLE 2

Barometric Pressures at Pressure Altitudes and Related Changes in Partial Pressures of Oxygen, Percentage Saturation of the Blood and Functional Disturbances Breathing Air

Pressure Altitude in Feet	Barometric Pressure in mm.Hg	Oxygen Partial Pressure in mm.Hg				Average Percentage Oxygen Saturation of Arterial Blood†			Effect
		Inspired Air*	Alveolar Air†			Max.	Av.	Min.	
			Max.	Av.	Min.				
Ground	760.0	159							
1,000	732.9	153	118	102	74		97.4		
5,000	632.3	132	94	82	72	89	91.0	93	Reduced night vision.
8,000	564.4	118	69	65	59	87	89.0	92	Fatigue in flights over four hours.
10,000	522.6	110	72	61	43	82	85.4	89	Construction of dyna- mic visual field (daylight).§
12,000	483.3	101	61	51	39	81	84.9	89	Fatigue, headache, errors in judgment, indifferent mental condition de- creased work ca- pacity.
15,000	428.8	90	60	44	33	70	74.4	78	Gross mental abnor- mality . Early con- vulsions in some.¶
18,000	379.4	79	48	38	30	77	71.2	65	Rapid loss of muscular control.
20,000	349.1	73	44	35	27	76	70.8	65	Collapse imminent.
25,000	281.9	59	34	32	31				
30,000	225.6	47							

*Calculated. †Subjects acclimatized at 1000 feet (Allan 1945). ‡Subjects at rest breathing air after 15 to 30 minutes at simulated altitude (Armstrong and Heun, 1937). §(Armstrong, 1939). ||(Aviation Medical Service Bulletin, 1947). ¶(Baxter et al., 1944).

that of the resting state. If the carbon dioxide level in the blood falls, however, acapnia may ensue, but in moderate hyperventilation the increased respiratory exchange serves, along with an increase in heart rate, usually, but not always, as a compensatory mechanism for combating hypoxia. Severe anoxia, however, produces periodic breathing and eventually respiratory arrest.

The above data direct attention to the importance of changes in vital capacity of the lungs, or variations from whatever cause in the ratio of residual air to total capacity. A decrease in vital capacity can only adversely affect one of the important

physiological mechanisms for acute adaptation to altitude. Bloomer (1947), reviewing the problem of tests of use in the evaluation of pulmonary pathology, reproduces data of Bowen and Platt (1923), which are presented here to show variations in vital capacity with age (fig. 1). A decrease in vital capacity of from about 15 to 55 per cent. is seen at the age of sixty-five years, and the mean figures show a decrease with age which is significant after approximately the age of forty-five years. This means that on the average, individuals over forty-five are less adaptable to hypoxia than are younger persons. The work of Berg (1947), dealing with respiratory gas exchange at ground level, after moderate exercise, also shows large variations with age in the time constants of recovery curves for oxygen consumption and carbon dioxide elimination. The "carbon dioxide constant" increases in the order of 100 per cent. over the age-groups twenty to sixty years, and the "oxygen time constant" increases in the order of 80 per cent. over the same age-range. The changes in vital capacity with age mentioned above or in pulmonary fibrosis, emphysema, pneumothorax, and atelectasis may well be one factor in producing the results reported by Berg, an influence which he speaks of as the "unloading capacity of the lungs". Other factors,

such as physical fitness, blood volume, cardiac output, haemoglobin content, biochemical variations of the blood, and pulmonary membrane pressure-gradients no doubt are involved. Data similar to those of Berg obtained at altitude over a significant age-range in normal and pathological conditions would be of considerable value.

The quantitative definition by Lilienthal and Riley (1946), and Lilienthal, Riley and Proemmel (1945-6) in man of the oxygen pressure gradient from alveolar air to mixed arterial blood, and confirmation by Gemmill (1947), Houston and Riley (1947), and Lilienthal, Riley, Proemmel and Franke (1946) are a significant contribution to aviation physiology, and their papers give data both at ground level and at altitude under conditions of rest and work for healthy subjects from twenty-eight to thirty-six years of age. This research directs attention to the significance of distinguishing between the percentage saturation of arterial blood with oxygen, the oxygen capacity of blood, and the partial pressure of oxygen in the blood. The latter factor deserves much attention because the magnitude of the oxygen pressure-gradients does much to define the rate of transfer of oxygen from the inspired air through the lungs, blood, and into and along the tissue oxidation enzyme systems; that is, the tissues "operate"

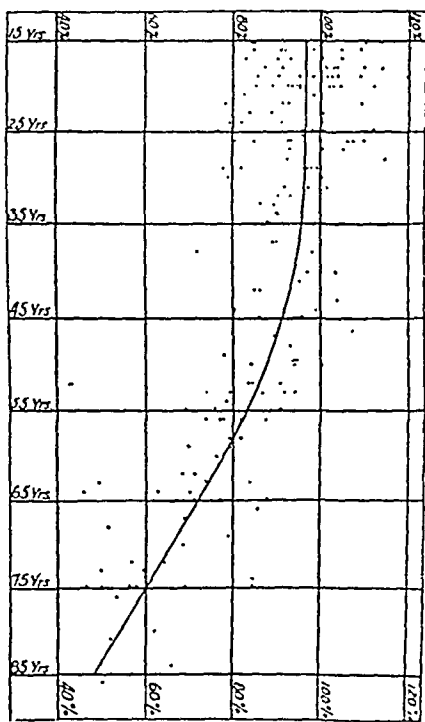


FIG. 1.—Chart taken from Bowen and Platt (*Yale J. Biol. Med.*, 20, 139, Dec., 1947) showing changes in vital capacity with age.

on a pressure basis rather than on percentage saturation figures. The effect of carbon dioxide on the haemoglobin dissociation curve, and hence on the partial pressure of oxygen, is of considerable importance, and more emphasis in the future should be placed on local conditions existing in the individual tissues where vital oxidation actually takes place. This view has been emphasized in an excellent paper by Poulton (1939). Fig. 2, from the work of Lilienthal and Riley (1946), is reproduced to illustrate some of the factors in oxygen transfer from the alveoli to arterial

THE FLOW OF OXYGEN FROM INSPIRED AIR TO ARTERIAL BLOOD

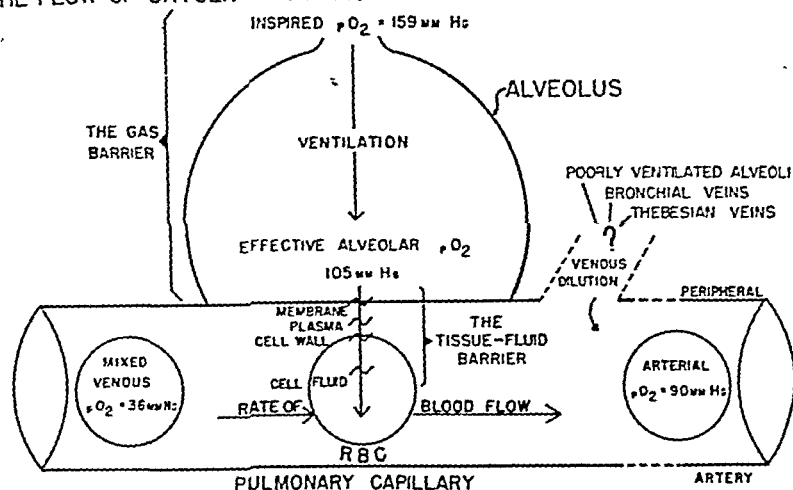


FIG. 2.—Taken from Lilienthal and Riley, showing some factors concerned in the transfer of oxygen from the alveoli to arterial blood. (Research Report No. 3 on Project No. x-484 (AV-258-f) Naval School Aviation Medicine, Pensacola, Fla., dated 23 February, 1946.)

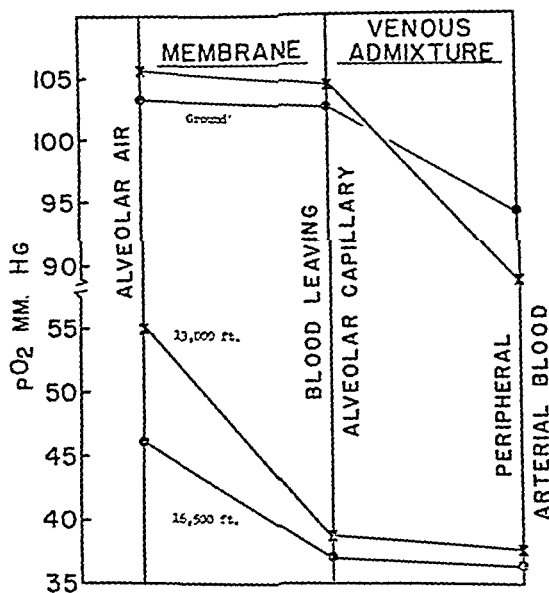


FIG. 3.—Chart taken from Lilienthal and Riley showing the oxygen tensions which obtain from alveolar air to peripheral arterial blood. X = exercise. • = rest. (Research Report No. 3 on Project No. x-484 (AV-258-f) Naval School Aviation Medicine, Pensacola, Fla., dated 23 February, 1946.)

blood, and fig. 3, slightly modified from Lilienthal and Riley (1946), shows the quantitative range of the results at "sea" level and simulated altitudes (oxygen-nitrogen mixtures of 13,000 feet and 16,500 feet).

It can be seen that the oxygen pressure-gradient across the "pulmonary membrane" is relatively small at ground level, even with exercise, but becomes relatively large at altitude, especially under conditions of muscular activity. If one assumes that individuals with certain types of pulmonary pathology would have higher than normal oxygen pressure-gradients from alveolar air to arterial blood, then data in fig. 3 mean that the oxygen pressure in arterial blood can be expected to drop very sharply at altitude in these cases. Quantitative investigation of this point is needed. Although the analysis of Lilienthal and co-workers (1946) has not

neglected the influence of the Bohr effect on oxygen partial pressures, it is difficult to say how this factor will behave in instances of pulmonary pathology. The effect of the alveolar carbon dioxide on the hæmoglobin dissociation curve is of paramount importance to tissues from which the venous blood is highly desaturated; that is, some tissues cannot compensate by extracting a greater amount of oxygen from the blood as is the case with striated muscle. One of these tissues is the heart.

EFFECT OF ANOXIA ON THE HEART

The cardiovascular events stated to follow exposure of humans to lowered partial pressures of oxygen (equivalent to about 15,000 feet) involve an increase in pulse rate, a rise in systolic pressure, no change, or slight rise or fall, in diastolic pressure, an increase in cardiac output, and a deduced dilatation of the coronary blood vessels without which the known compensatory reactions of the heart could not occur (Wiggers, 1941). This author describes a point in progressive hypoxia at which "crisis" occurs. The pulse rate and blood pressure fall, systolic discharge fails, venous pressure climbs sharply, disturbances in conduction and rhythm occur, and congestive heart failure ensues, usually, however, much later than the onset of unconsciousness. This "typical" or "average" picture in a young man with a "healthy" heart may be misleading. Those who have worked in low-pressure chambers during the past war know well that the so-called crisis is often seen at relatively low altitudes (14,000 to 18,000 feet) and most often in individuals who do not show a rise in pulse and blood pressure. This failure to show cardiovascular adaptation is consistently seen in some persons, and also a wide variation in the "normal" response to hypoxia in other men. Such reactions have been observed by workers using the Levy test (breathing 10 per cent. oxygen and 90 per cent. nitrogen mixtures) for diagnostic purposes (Burchell, Pruitt and Barnes, 1948). The reasons for this are not clearly understood.

Motley *et al.* (1947), using intracardiac catheterization in conscious men, twenty-three to forty-seven years of age, measured the blood pressure in the pulmonary artery during inhalation of 10 per cent. oxygen in nitrogen for brief periods of time. These workers reported a significant but reversible degree of pulmonary hypertension during the period over which 10 per cent. oxygen was breathed. A slight decrease in cardiac output, increase in heart rate, decrease in stroke volume, increase in pulmonary ventilation, a marked rise in pulmonary vascular resistance and a slight increase in systemic vascular resistance were also observed. The rise noted in pulmonary vascular pressure, and decrease in cardiac output are surprising, and the former, if confirmed, is a significant fact, not only in aviation physiology, but in the field of surgery.

Levy and his co-workers (Patterson, Clark and Levy, 1942) first used the "anoxæmia test" on normal subjects and patients with coronary sclerosis. Pruitt, Burchell and Barnes (1945, 1948), who reported on 730 tests carried out at the Mayo Clinic, are inclined to believe that positive tests are related to inability of the coronary vessels to allow the tremendous increase in flow that normally takes place, but that other factors play an important part in some cases; that is, variations in redistribution of coronary flow and drainage and the amount of coronary vasoconstriction; also, there are positive tests

in only 50 per cent. of individuals in whom the clinical diagnosis of coronary sclerosis has been made (Burchell, Pruitt and Barnes, 1948).

Although the nature of the effect of hypoxia on the *ageing heart* cannot be stated with certainty, it is significant that the Mayo men recommend that the test should not be done in men over sixty years of age or in those with a previous myocardial infarct, and they terminate a test a few minutes after the physiological unsteady state which exists during the procedure has progressed to the stage in which there is blood oxygen saturation of 70 to 75 per cent. It is well to recall that the arterial partial pressure of oxygen may vary about 15 mm. Hg at a blood oxygen saturation of 70 per cent. with a shift in pH from 7.2 to 7.4 (Best and Taylor, 1940). The anoxic strain on the heart in cases in which a respiratory (or local) alkalosis exists may be more severe than the percentage oxygen saturation might indicate. Also, the venous blood from the coronary sinus is reported to have oxygen saturations as low as 10 per cent. (Burchell, *et al.*, 1948), and the myocardium is therefore likely to be materially embarrassed by either a decrease in coronary flow or a decrease in the arterial partial pressure of oxygen. The latter, as already noted, can be intimately related to chest pathology.

Hammonds (1944) reported one case of myocardial infarction with recovery which occurred in a twenty-year old male following exposure to simulated altitudes of 38,000 feet with oxygen and 17,000 feet without oxygen inhalation, in a routine altitude indoctrination run in a low-pressure chamber. There was a previous history of mild hypertension.

The importance of these data relevant to hypoxia, to certain airline passengers, cannot be over-emphasized. Nine known deaths due to causes other than aircraft accident occurred on airlines in the United States between June and October, 1947 (Aviation Medical Service Bulletin, 1947).

Three were proven by autopsy to be due to coronary occlusion. Two of these three occurred at altitudes of 6000 and 7000 feet. The third was on an overseas flight at an unknown altitude. There were no autopsies on the other six deaths. One of these was listed as due to heart failure at 7000 feet. Another was tabulated as caused by heart disease, and occurred in a pressurized plane flying at 19,000 feet with a cabin altitude of 7,800 feet. The cause of death in three cases was listed as unknown at cabin altitudes of 8000 to 11,000 feet, 6000 feet, and 7000 feet, and the last death was said to be due to cerebral hæmorrhage and dilatation of the heart in a pressurized plane cruising at 18,000 feet with a cabin altitude of 7,100 feet.

It is true that these deaths could have occurred on trains, buses, or at home, but a passenger psychologically prepared for flight and using oxygen prophylactically would probably be better off in an airplane than travelling by any other means. It is the responsibility of the family doctor to advise prophylactic oxygen, when indicated, for his patients who wish to fly even at relatively low altitudes, and it is the obligation of the airline to make adequate equipment available over the entire trip. Most airline companies are anxious to cooperate in special cases. Their problem is to know which passengers are in need of oxygen inhalation. In the United States, the regulations of the Navy and Army Air Forces require oxygen use at 8000 feet* and above for flights of more than four hours' duration and at all

* Operating personnel are required to use oxygen from the ground up at night.

times above 10,000 feet. Some hold that oxygen is unnecessary in cases of cabin pressurization failure at altitudes of 18,000 to 22,000 feet, provided the aircraft be brought to 14,000 feet within four to six minutes. This is probably a safe assumption if the passengers are "normal". It is our opinion that the oxygen rules enforced by a few airlines should conform to the following for all airlines (Lovelace and White, 1947):—

(1) Oxygen should be used by all passengers and aircrew at all times above 12,000 feet.

(2) Oxygen should be used by all aircrew at altitudes between 10,000 and 12,000 feet during that portion of the flight in excess of thirty minutes within this range of altitude.

(3) In pressurized aircraft, oxygen should be used by each member of the crew and by all passengers in case of pressurization failure, as stated in paragraphs 1 and 2 above.

(4) All aircraft should carry emergency oxygen at all times for the aircrew and for at least 10 per cent. of the passengers.

(5) Some provision should be made to make possible the administration of increased oxygen flow to cardiac patients and other individuals when indicated.

(6) A satisfactory means for dispensing oxygen to infants should be provided in all aircraft.

The above opinion represents a practical compromise with recognized problems relevant to airline operations and is about "2000 feet above" the oxygen altitude indicated by the best scientific data. Under these conditions, it is important that the practitioner be as professionally active as possible in protecting his flying patients, and politically active in urging the adoption of safe regulations by civil aviation authorities.

Experience has shown that the anoxic hazard is enhanced by alcoholic intoxication, liver disease, anæmia, late pregnancy (last trimester), epileptic tendencies, psychopathic states, emotional disturbances, fright, infections, and fatigue. Diets high in carbohydrates, on the other hand, are reported to decrease the deleterious effects of anoxia (King, *et al.*, 1945; Green, Butts and Mulholland, 1945; Eckman, *et al.*, 1945).

The *hyperventilation syndrome* (Rushmer, Boothby and Hinshaw, 1941) is a group of symptoms caused by a respiratory alkalosis due to loss of blood carbon dioxide during increased respiratory minute volume. The etiology as a rule is anxiety, fright or nervousness, and maybe hypoxia, or can be entirely voluntary. The symptoms include numbness and tingling of the forearms, hands and legs, vertigo, faintness, pallor, muscular cramps, especially tonic carpopedal spasms, periodic breathing, acapnia, pallor, collapse and unconsciousness. The symptom complex has been observed by Uihlein and Boothby (1942) in airline passengers, and in aviators by Beckman (1945). Relevant information was included in Army and Navy pilot training programmes. Symptoms are much more likely to occur at altitude than at ground level. Treatment is carbon dioxide administration when available, rebreathing expired air, breath-holding, and voluntary slowing of ventilation volume. The syndrome, through acapnia, can produce anoxia at altitude. This may be of sufficient magnitude to affect some passengers seriously.

DISTURBANCES DUE TO VARIATION IN BAROMETRIC PRESSURE

Gas volume at constant temperature varies inversely with the barometric pressure according to the law of Boyle, and the quantitative changes with

variations in altitude are shown in fig. 4. If changes of volume cannot occur, corresponding pressure variations ensue. The effects seen in man during flight involve variations in the volume or pressure of gas contained in (1) the body cavities, and (2) the tissues.

(1) *Body cavities*

Gas-containing body cavities of significance in aviation are the ears, paranasal sinuses, the gastro-intestinal tract and, in some pathological instances, mediastinum, the pleural and peritoneal cavities.

Aerotitis media is a clinical entity, the symptoms of which are due to

failure of the air pressure within the middle ear to follow the ambient barometric variations during changes in altitude (Armstrong, 1937, 1939). On ascent, there is some outward bulging of the tympanic membrane and then medial movement when air escapes along the Eustachian canal. During descent, however, marked and alarming symptoms may occur if gas does not re-enter the middle ear through the Eustachian tube. In normal individuals, the patency of the Eustachian canal is to some extent under voluntary control. The occurrence of aerotitis media is sometimes due to failure to swallow, yawn, and to perform other manœuvres which activate

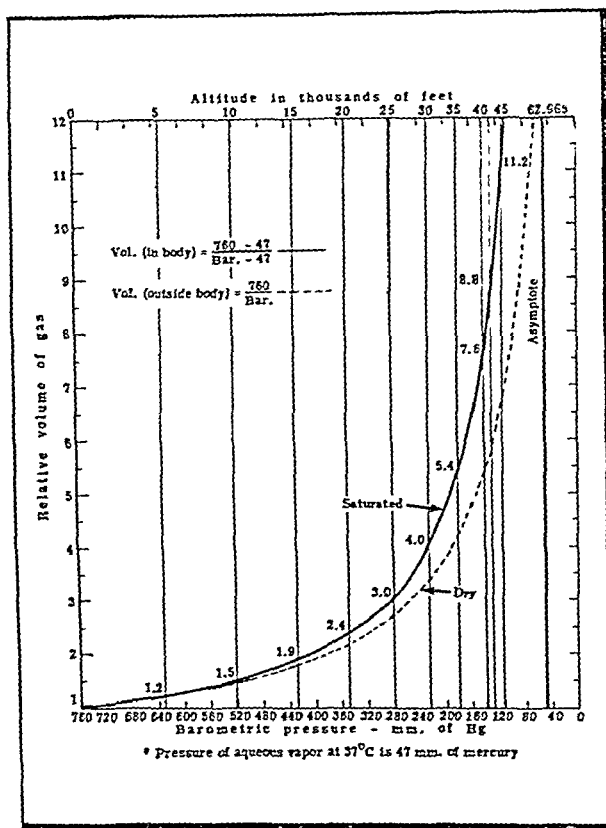


FIG. 4.—Chart taken from "Physiology of Flight" showing variations in relative volume of gas with changes in barometric pressure. ("Physiology of Flight." AAF Manual No. 25-2, Aeromedical Laboratory, Wright Field, Dayton, Ohio, 15 March, 1945.)

the veli palatini muscles which aid in opening the Eustachian tube. Other etiological factors in tubal blockage involve enlargement of pharyngeal and Gerlach's tonsils (Armstrong, 1937, 1939), lymphoid hypertrophy within the lumen of the canal (Fowler, 1946), thick mucus present over the pharyngeal orifice of the Eustachian tube, membrane turgescence due to upper respiratory infection and allergy, sinusitis, post-nasal discharge, anomalies in dental occlusion (Bierman and Brickman, 1946), especially overbite, and tubal stenosis.

Signs and symptoms of acute aerotitis include ear pain, often excruciating, loss of hearing, retraction and marked injection of the membrane tympani, sometimes with hæmorrhage within the drum substances, fluid in the middle ear, often blood-stained, and occasionally rupture of the ear drum. Purulent otitis media is a rare complication in adults (White, 1943-7). In chronic aerotitis media, a thickened, dull, lustreless drum with diminished or absent light reflex and retraction, and occasionally bulging, may be seen. The torus tubarius of the Eustachian tube usually shows the presence of a chronic inflammatory process, and prominent tubal cushions are common. Signs of tubal stenosis are less often encountered. Subjective complaints involve a decrease in hearing, first involving low tones, occasionally vertigo and tinnitus, and a "stuffy and full" feeling in the ears.

In *treatment of aerotitis*, prophylactic measures are most effective. Upper respiratory infections contraindicate flying, as does an inability to perform the Valsalva manœuvre with gentle pressure before flight. Individuals need to be taught how to ventilate the ears, to do so when descending in flight at least once during a loss of each 500 feet in altitude, and in cases of sluggish tubal ventilation to use the Valsalva manœuvre gently *before* ear pain occurs and, when other measures fail, to relieve the increasing pressure on the ears. Pressurized aircraft minimize the occurrence of ear symptoms, as does slow descent in flight. Correction of dental malocclusion may be necessary and is important in preventing hearing loss in some persons.

Immediate treatment of *acute symptoms* should be conservative. Pain, if severe, must be relieved with morphine, if necessary; sedative ear drops and heat, especially diathermy, are helpful. Decongestants placed near the tubal opening are indicated. Some authors recommend inflation of the middle ear by catheterization and politzerization (Lentine, 1946). This is seldom necessary and is likely to traumatize the tubal tissues in the region of the ostium. It is our practice, when inflation seems absolutely necessary, to pierce the drum with a 25 gauge hypodermic needle after instillation of antiseptic and anæsthetic solutions in the middle ear. Cases in which symptoms do not clear up within three to four days should be referred to a specialist for treatment, especially if fluid persists in the middle ear.

Treatment of *recurrent otitis media* by irradiation often yields dramatic results. Morris (1945) has discussed the use of X-rays, and the excellent paper by Fowler (1946) presents facts relevant to the use of radium, as do a series of publications by Army Air Force personnel (Mikell, 1945; Hendricks

and Lieberman, 1945; Collins, Eschenbrenner and Lyle, 1945; Weymuller and Magnuson, 1945). The proper use of radium in the nasopharynx deserves a much wider general application, especially as prophylaxis against deafness, which develops as a sequel to changes in the Eustachian tube following recurrent attacks of otitis media.

Aerosinusitis has been discussed by Campbell (1942) and Dickinson and Voelker (1945). Symptoms are produced by failure of air to re-enter the sinuses under increasing ambient pressure (descent in aircraft, submarines or caisson workers, but occasionally may occur during ascent in aircraft). Upper respiratory infection, flying with colds, allergy, acute or chronic sinusitis, malformation of the nasal septum, and polypi are most important etiologically. The frontal and maxillary sinuses are most frequently involved. Pain, often very severe, is the most prominent complaint. Examination of the nose reveals the usual signs of congestion and sinusitis. Transillumination and X-ray studies of the sinuses may reveal thickened membranes, poor aeration of sinus, a fluid level, and hæmatoma (Dickinson and Voelker, 1945). Cases with blood-stained discharge containing strips of mucous membrane have been seen (White, 1943-47). Presumably redundant tissue or thick mucus block the opening into the sinus, or the turgescient membranes about the sinus ostia are evaginated inward, and the barotrauma actually produces tearing of the tissue followed by hæmorrhage into the sinus cavity.

Treatment is avoidance of flying, rest, measures to allow proper drainage and aeration of the sinus, and therapy of the underlying condition. Nasal sprays, when properly used, are effective in relieving immediate symptoms, and of value in individuals with chronic sinusitis who must fly.

Gas present in the gastro-intestinal tract seldom causes symptoms in apparently normal individuals until altitudes of over 30,000 feet are reached, and is no significant problem in the commercial airline passenger to-day. However, in the presence of gastro-intestinal infections, cardiospasm, obstruction and megacolon, symptoms may occur. Collins (1941) described a case of the latter condition in a twenty-three year old air passenger who noted symptoms of dyspnœa, præcordial pain, and swelling of the abdomen at 14,000 feet. In the presence of some gastro-intestinal anomaly, which prevents deflation, such as a rectal obstruction with a competent ileo-cæcal valve, abdominal gas may produce difficulties in an air passenger.

Pulmonary affections.—Considerable care on the part of physicians is indicated in advising potential air passengers when pneumothorax, diaphragmatic hernia, and mediastinal emphysema exist. Lovelace and Hinshaw (1942) and Bridge and Bridge (1945) have discussed the problem, and Dowd (1945) has described a fatal incident in an air passenger in which pneumothorax was a prominent factor. Lovelace and Hinshaw (1942) give ample X-ray evidence showing that altitudes between 5000 and 12,000 feet produce a pronounced increase in the size of a pneumothorax. Pressure changes in patients with adhesions in the pleural cavities may result in

effusions, rupture, and hæmorrhage. It is important to realize that the total pressure within the pleural cavity is a function of the area involved and that an adhesive band and the mediastinum may be subjected to significant displacement or stretching.

Aerodontalgia, or pain in or about the teeth, associated with changes in barometric pressure, has been reported to have an incidence of from 1 to 5.8 per cent. of individuals exposed in low-pressure chambers (Hutchins, *et al.*, 1945; Stewart and Macintosh, 1945; Kennon and Osborn, 1945; Weiner, 1944), and is higher for civilian than for military personnel. The affliction has occurred at altitudes as low as 2000 feet. In the series of Stewart and Macintosh, 32 cases were reported below 20,000 feet, and 31 cases between 20,000 and 25,000 feet. Symptoms may occur either on ascent or descent, and the exact cause of the entity is not clear. Etiological factors appear to include restorations, especially if done without insulation, infection in the root canal, periapical abscess, aerosinusitis, pulpitis, caries, recession of gums, radicular cysts, impactions, and pulpstones. It is likely that those cases which occur on descent have aerosinusitis prominent in the etiology.

The leading symptom is pain. This may be sharp and severe, well localized and incapacitating. A dull ache, poorly localized, may be felt alone or after sharp, well-defined pain. Occasionally, swelling about the teeth and jaw occurs, and toothache may persist after exposure, often due to the presence of apical abscess, although pain usually subsides spontaneously.

Treatment consists in correction of the underlying cause of the condition; pain, occurring in repeated exposures, should always indicate dental consultation. The fact that men with aerodontalgia can have deep fillings removed and replaced after proper insulation (zinc oxide and eugenol, pulprotex) of the cavity, and be exposed to high altitude the next day without pain, indicates that dental procedure satisfactory at ground level, is often not satisfactory at altitude.

(2) *Gas in the tissues*

Disturbance due to expansion of gas in the tissues of the body when exposed to a decreased barometric pressure involves the very broad problem of decompression sickness. Although this highly interesting entity involves symptoms referable to the skin, the bones, joints and tendinous areas, the chest, the nervous system, and sometimes post-exposure reactions with serious implications, it is unlikely to be a problem in commercial air passengers except on rare occasions, because symptoms do not occur with any significant frequency below 20,000 feet. Allan (1945) described instances of pain similar to that noted in "aviators' bends" located near areas of traumatic calcification, aseptic necrosis, myositis ossificans, and in the hip of an individual with hypertrophic changes in an old Legg-Perthes' disease of the hip. In two of these cases symptoms occurred repeatedly at altitudes as low as 10,000 and 15,000 feet. In view of the well-known

sensitivity of certain arthritics to changes in barometric pressure, it is highly probable that many unreported instances of joint pain during air travel exist. Data relevant to this might be significant in evaluating progress in selected cases of the arthritides.

CHANGES RELATED TO CHANGES IN TEMPERATURE

The temperature of the atmosphere decreases with increasing altitude. The approximate fall is 2°C . for every 1000 feet, although considerable variation occurs. For example, measurements over San Diego, California, at 40,000 feet revealed temperatures in the range of -40°C . to -80°C . (A.A.F. Manual, 1945). Modern aircraft are equipped with heating and ventilating systems which are fairly adequate, but it is not uncommon for an unpressurized airplane at a desert or tropical airport to be almost unbearably warm, to be uncomfortably cool in flight and to land several hours later in areas with arctic temperatures and winds. Air travellers, especially the debilitated and aged, should prepare for such exigencies by proper dress.

SAFETY MEASURES

Effects of motion.—Since motion sickness is being discussed elsewhere in this issue by Professor Noble, no remarks will be made except to say that in our opinion the problem is a very real and important one in commercial flying, and means are at hand to control a high percentage of motion sickness occurring in airline passengers. Although the advent of the higher flying pressurized aircraft *have all but eliminated* the problem over routes where "over-the-weather" flying is scheduled, it is the medical profession's obligation to see that a satisfactory way is found to get effective remedies for air sickness into the hands of the flying public, not forgetting those unfortunate individuals who suffer from car, sea, and train sickness.

The most important aspect of acceleration and deceleration in commercial aviation is not the "positive" and "negative" "g" on which so much significant work was done during the war, but the results of linear or transverse "g" as encountered in air crashes. DeHaven (1942, 1944), in his important studies, has pointed out that man can tolerate decelerative forces of 200 "g" briefly, acting transversely in the long axis of the body. This is well above the decelerative forces acting on many structural components of aircraft, especially those aft of the wings, during crash. DeHaven (1942, 1944) also points out, as emphasized by Wilson and Helmholtz (1945), that the "whip" action of the trunk confined by a safety belt, propels the head into solid structures with a force much greater than that actually placed upon the body of the airplane at that point during a crash. In 200 of 554 deaths in airplane accidents in which severe burns of the body occurred, 504 were due to fatal crushing injuries to the head and trunk with burns secondary to the injuries. When it is possible to state that the "prevention of crushing injuries is 40 times as important as fire prevention in eliminating passenger deaths in crashes which involve fire", it is time to pay close attention to the design of commercial aircraft to take advantage of the facts. Two important

features belong in the design of all future aircraft, namely, (1) properly constructed seats, well anchored to the main structural elements of the aircraft, and of sufficient strength and location to give occupants minimal exposure to decelerative forces, and at the same time maximal distribution of this force transversely to the long axis of the body; (2) escape hatches of sufficient number and size to allow quick escape of survivors from fire. The latter involves emergency windows with minimum dimension of 18 inches square (Wilson, 1945). The former points to *backward* facing seats, high enough to support the head and located as far aft of the wing as is feasible. DeHaven (1945), of Cornell University, in a report to the Civil Aeronautics Board, emphasized the "safety resulting from slightly rearward positions" in the aircraft as "very marked". Ditching procedures in aircraft during the past war also lend strong support to the contention that the properly positioned and supported human body has a well-enhanced chance of survival. McFarland (1946) also strongly favours this view.

There is no doubt but that *rearward* seating is the *safest* seating. There are no valid arguments to deny this, but there is much resistance among engineers, who say that many people will object to riding backwards. This is not a proven fact. There is little sense of relative motion in flight; visibility from most current aircraft is better looking aft of the wing; many individuals ride backwards in trains and in some automobiles, and there is no reason to anticipate any adverse physiological effects of backward motion. What psychological factors or acceptability resistance the passenger public might show can be overcome by a world-wide educational programme giving the factual data relevant to safety. This should be initiated now and, if successful, will mark a significant advance in aircraft safety.

Toxic gases.—A number of current airliners utilize the energy contained in exhaust gases for cabin heating. Such systems constitute a slight hazard even if properly maintained and tested frequently, for breakage or rupture of portions of the ducting elements can occur in flight. For this reason, and because of possible *carbon monoxide* production from in-flight fires, many aircraft contain carbon monoxide warning systems; when properly serviced, these work very well to afford ample warning of danger. Because of the hæmoglobin-binding property of carbon monoxide, toxicity is much enhanced at altitude, and concentrations in flight should not exceed 0.0025 to 0.005 per cent. The carbon monoxide hazard is much more likely to occur in private, single engine planes with improperly designed exhaust stacks and poorly sealed cabins. A pilot who appears "drunk" after flight deserves a blood test for carbon monoxide, as well as for alcohol, and a doctor, as shown in many instances in military experience, can do much to protect men from unfair charges and convictions.

The toxic effects of *carbon dioxide* at both ground level and altitude deserve more study (White, 1948). Although direct evidence in the literature is meagre, a recent review of the problem (White, 1948) tentatively fixed the maximal safe allowable carbon dioxide concentration at ground level at

5 volumes per cent. for 5 minutes or less, 4 volumes per cent. for 15 minutes or less, and 1 volume per cent. for not more than two hours. Carbon dioxide is better tolerated at altitude, and tolerance, being a function of the partial pressure, allows calculation of altitude equivalents from the ground level data. Four volumes per cent. carbon dioxide at ground level, for example, is equivalent to 5, 6, and 7.5 volumes per cent. at pressure altitudes of 5000, 10,000, and 15,000 feet, respectively. It is known that most modern airliners carry considerable carbon dioxide for fire-fighting purposes, and that some have been tested in flight against hazardous carbon dioxide concentrations. It is doubtful whether the problem has had widespread appreciation, since no relevant civil regulations exist. Carbon dioxide in sufficient concentration is quite toxic to humans, and all commercial aircraft carrying this gas should be thoroughly flight-tested.

Fire extinguishers containing carbon tetrachloride are carried in many aircraft. It is doubtful if they are safe for in-flight use in inhabited compartments of the plane. Sollman (1948) states that a concentration of 0.1 volume per cent. in air is unsafe, and that when heated to over 200° F. (93.3° C.) phosgene gas may be produced, and that fatalities have occurred from phosgene production in confined space. No ideal fire-fighting agent for use in inhabited compartments of aircraft in flight is available. This problem deserves careful attention. Meanwhile, the use of water on selected cabin fires has great advantages over employment of the more toxic agents.

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EPIDEMIOLOGY AND AIR TRAVEL

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THE speed of modern air travel has resulted in problems concerning the transference of diseases which were never present in the older and slower forms of transport. In the case of travel by surface transport, the time taken in travelling from an endemic to a non-endemic area was usually adequate for the manifestation of symptoms *en route*, and therefore appropriate action could be taken before passengers were allowed to disembark, to ensure that no infected personnel introduced disease to another country. With air travel this no longer applies, and a passenger from an endemic area may well be incubating a disease for several days and infecting other persons before symptoms become manifest. For example, using air travel, this country can now be reached from Egypt in thirteen hours, West Africa in a day, India in a day and a half, and China in six days. It is therefore apparent that medical authorities will have increasing difficulty in ensuring that passengers arriving in a country by air are not incubating an infectious disease. As a result greater reliance will have to be placed on immunization by internationally approved methods, the burden of proof of such action having been taken being the responsibility of the passenger concerned.

INTERNATIONAL CONTROL

The prevention of spread of infectious disease from one country to another is controlled by regulations drawn up by the International Convention for Aerial Navigation of 1944 (I.C.A.N.). This convention defines the procedure and methods to be adopted by the signatories for the purpose of quarantine. Such methods include immunization against the five major epidemic diseases, yellow fever, smallpox, plague, typhus, and cholera, together with medical supervision of any suspected travellers and segregation of any proven cases or contacts. In addition to these measures it will be necessary to ensure that aircraft, crew, and passengers are not carriers of such diseases, by the application of adequate sanitary measures, including methods for the destruction of mosquitoes and other disease vectors.

EFFECTIVE VALIDITY OF IMMUNIZATION PROCEDURES

The incubation periods for these diseases and the periods of validity of the certificates of immunization agreed on internationally, are as indicated in the tables 1 and 2 (page 438).

In spite of these internationally agreed periods of validity, foreign countries often promulgate amended requirements at short notice. Instances of recent variations are recorded in table 2, and are subject to frequent

amendment. Both limits of validity should be noted on making arrangements for immunization. The consequences to a passenger who is not in possession of valid certificates may be a refusal to permit embarkation, or an enforced period of quarantine at the port of disembarkation, or in some instances a refusal of permission to land.

TABLE 1

<i>Disease</i>	<i>Incubation period</i>	<i>Periods of validity of immunization certificates</i>
Yellow fever	6 days (India 9)	10 days to 4 years from date of inoculation
Smallpox ..	14 days ..	14 days to 3 years from date of vaccination
Cholera ..	5 days	6 months from date of inoculation
Plague ..	6 days	Not stated, but usually 6 months from date of inoculation
Typhus ..	12 days	1 year from date of completion of course of inoculations

HEALTH REGULATIONS IN DIFFERENT COUNTRIES

The extent of immunization which is necessary depends upon the route to be flown. The current regulations of each country touched in transit, as well as those of the country of departure and destination, must be observed.

TABLE 2

<i>Disease</i>	<i>I.C.A.N. validity</i>	<i>Limits of variation</i>	
		<i>Maximum</i>	<i>Minimum</i>
Yellow fever	10 days/4 years	16 days/2-4 years (India)	15 days/2 years (Madagascar)
Smallpox	14 days/3 years	14 days/3 years (Egypt)	15 days/6 months (Thailand)
Plague	None stated	6 days/2 years (Cyprus)	6 days/3 months (Hong Kong)
Typhus	1 year	12 days/1 year (Lebanon)	9 days/6 months (Cyprus)
Typhoid	None stated	6 days/1 year (Burma)	6 days/3 months (Java)

In certain cases authorities permit relaxation of these rules when a passenger is in transit through a country, but in such cases movements during the period of waiting may be limited. In addition to the inoculations and vaccinations required by quarantine regulations certain others are recom-

mended as an additional precaution. Inoculation against the typhoid group should be recommended to any person going abroad, but other inoculations need only be advised when epidemics are known to be in progress, and information on this question can be ascertained from the Unit Information Service, Airways Terminal, Victoria, London, S.W.1 (telephone, Victoria 2323), and will probably in due course appear regularly in the current medical journals. It is understandable that those countries which are free of particular diseases but whose terrain and climatic conditions are particularly favourable for its spread should exercise stringent precautions to prevent the entry of carriers of such a disease. Thus the regulations against the importation of yellow fever into India at present are very strict, and the same observations apply with regard to smallpox in Australia.

HEALTH REGULATIONS ON ARRIVAL FROM A FOREIGN COUNTRY

Certain countries require passengers to give an account of their movements during the fourteen days before disembarkation. The purpose of such an inquiry is to establish their whereabouts during the period covering the longest incubation period, namely that of smallpox. Should they fall ill within the subsequent twenty-one days they are instructed to report to the nearest doctor with a warning card issued to them on disembarkation which states that the holder has recently arrived from another country, and may be suffering from a notifiable infectious disease. In addition, the local Medical Officer of Health is informed by the Health Officials at the airport of disembarkation of any cases which have arrived. Passengers who have been in contact with an infectious disease or who are suspected of having contracted it may be required to undergo a medical inspection, followed by observation in a hospital or surveillance at their place of residence. It may also be required that their persons and personal effects are cleansed or disinfected according to the circumstances.

CLINICAL DETAILS OF INOCULATIONS AND VACCINATIONS

The following details of dosages for inoculations are recommended officially at the present time:—

YELLOW FEVER

Certain vaccines only are recognized internationally for inoculation against yellow fever, and in this country they are prepared at the Wellcome Research Institute, London. The vaccine must be kept at a temperature between 0°C. and 4°C., and the dosage made up for injection with water or normal saline.

Dosage.—One injection of anti-yellow fever vaccine.

Adult	0.5 c.cm.
Children under 2 years	0.15 c.cm.

CHOLERA

Two injections of anti-cholera vaccine at 10-day intervals.

Adults

1st dose	0.5 c.cm.
2nd dose	1.0 c.cm.

Children 6-12 years

1st dose	0.25 c.cm.
2nd dose	0.5 c.cm.

*Children 2-5 years**Vaccine 2/5th full strength*

1st dose	0.2 c.cm.
2nd dose	0.4 c.cm.

TYPHUS

Three injections of anti-typhus vaccine at 10-day intervals.

Adults and children over 5 years

1st dose	1.0 c.cm.
2nd dose	1.0 c.cm.
3rd dose	1.0 c.cm.

Children 2-5 years

1st dose	0.5 c.cm.
2nd dose	0.5 c.cm.
3rd dose	0.5 c.cm.

Children under 2 years

Only in the presence of an epidemic

1st dose	0.2 c.cm.
2nd dose	0.2 c.cm.
3rd dose	0.2 c.cm.

PLAGUE

Two injections of anti-plague vaccine at 10-day intervals.

Adults

1st dose	0.5 c.cm.
2nd dose	1.0 c.cm.

Children

This is not advised for children under 12 years of age, except in the presence of an epidemic, when it may be given to children from two years upwards.

1st dose	0.2 c.cm.
2nd dose	0.3 c.cm.

TYPHOID GROUP

Two injections of the alcoholized anti-T.A.B.C. vaccine at intervals of not less than 10 days.

Adults (male)

1st dose	0.25 c.cm.
2nd dose	0.5 c.cm.

Adults (female) or children over 12 years

1st dose	0.2 c.cm.
2nd dose	0.4 c.cm.

Children 6-12 years

Vaccine 2/5th full strength.

1st dose	0.25 c.cm.
2nd dose	0.5 c.cm.

Children 2-5 years

Vaccine 2/5th full strength.

1st dose	0.2 c.cm.
2nd dose	0.4 c.cm.

SMALLPOX

The method used is the making of one dermal scratch followed by the application of lymph, and subsequently making a second scratch through this lymph. The results should be recorded as primary vaccinia, accelerated reaction, or reaction of immunity.

The immunization procedures described are not recommended for children under two years of age except when specific conditions or regulations require it, but children under two years of age may be vaccinated against smallpox and inoculated against yellow fever unless there are medical contraindications.

OFFICIAL INOCULATION CENTRES

A list of official yellow fever inoculation centres, together with the names of persons authorized to sign the certificates, as approved by the World Health Organization is indicated below. In addition, the signatures of certain Medical Officers of the Airline Corporations are authorized by the World Health Organization.

ENGLAND

<i>Birmingham:</i>	Regional Blood Transfusion Centre, 17 Highfield Road, Edgbaston, Birmingham, 15.	Telephone Edgbaston 1182	Tuesday 2—3 p.m.
<i>Bournemouth:</i>	Dr. R. Vaughan Facey Burwood Glen, 13 St. Stephen's Road, Bournemouth.	Bournemouth 2815	
<i>Bristol:</i>	Regional Blood Transfusion Centre, Southmead Hospital, Bristol.	Bristol 68021-3	Tuesday 2—3 p.m.
<i>Cambridge:</i>	Regional Blood Transfusion Centre, Brooklands Avenue, Cambridge.	Cambridge 2536	Monday 2.30—3.30 p.m.
<i>Leeds:</i>	Regional Blood Transfusion Centre, Bridle Path, York Road, Seacroft, Leeds.	Leeds 45091-2-3	Friday 2—3 p.m.
<i>Liverpool:</i>	Drs. A. Adams and R. Seaton, School of Tropical Medicine, Pembroke Place, Liverpool, 3.	Royal 7611	
<i>London:</i>	The Wellcome Foundation, (Wellcome Road, Victoria, S.W.1.)	Euston 4477	Monday to Friday 10.30 to 12.30 p.m.
		Victoria 2323	
<i>Manchester:</i>	Regional Blood Transfusion Centre, Manchester Royal Infirmary, Oxford Road, Manchester, 13.	Ardwick 3832	Tuesday 2.30—3.30 p.m.
<i>Newcastle-on-Tyne:</i>	Regional Blood Transfusion Centre, 78 Jesmond Road, Newcastle-on-Tyne, 2.	Jesmond 2992	Monday 2—3 p.m.
<i>Oxford:</i>	Southampton Regional Blood Supply Depot	Oxford 61316	Monday 2—3 p.m.
<i>Plymouth:</i>		Plymouth 5021	
<i>Southampton:</i>		Southampton 76211	Tuesday 2.30 p.m.
<i>Truro:</i>		Truro 3029	Tuesday 10—11 a.m.
	(Dr. F. D. M. Hocking).		
	WALES		
<i>Cardiff:</i>	Regional Blood Transfusion Centre, 19 Newport Road, Cardiff.	Cardiff 4521	Monday 2.30—3.30 p.m.
	SCOTLAND		
<i>Aberdeen:</i>	City Hospital Laboratory, City Hospital, Urquhart Road, Aberdeen.	Aberdeen 2242	Thursday 3 p.m.
<i>Dundee:</i>	University of St. Andrews,	Ext. 11 Dundee 2144	(or by arrangement) Monday 2 p.m.
	free of charge.		
<i>Edinburgh:</i>	Edinburgh Regional Blood Transfusion Centre, 100 George Street, Edinburgh, 3.	Edinburgh 26931	Monday and Wednesday 2.30—3.30 p.m.
	(Dr. W. R. Logan).		
<i>Glasgow:</i>	Public Health Clinic, 20 Cochrane Street, Glasgow, C.1.	Glasgow Central 9600 Ext. 302	Friday 2.30 p.m.
	NORTHERN IRELAND		
<i>Belfast:</i>	Ministry of Health for Northern Ireland, Emergency Hospital, Musgrave Park, Balmoral, Belfast.	Belfast 67693	By arrangement with Medical Superintendent

Dublin:

EIRE
Moyné Institute of Preventive Medicine.
Prof. J. W. Bigger and Dr. W. Hayes
(This institute is at present named the
School of Pathology, Trinity College,
Dublin).

HEALTH MEASURES FOR AIRCRAFT

The structure of an aircraft renders it liable to harbour certain disease vectors in relatively inaccessible places, such as the wings, cargo holds, and fuselage. Infection may be carried by rodents, mosquitoes, or other insects, as well as by food, water, cargo, or sewage, and special precautions have to be taken to deal with such problems, quite apart from the routine measures for sterilization of water tanks, and other containers.

DISINSECTIZATION

The specialized process for dealing with mosquitoes and other insects is known as disinsectization, and regulations require that it shall be applied to any aircraft whenever it arrives at, or departs from, an airport in a yellow fever or malarial zone. The procedure is carried out in the absence of passengers and crew, but with cargo and fuel on board.

Technique.—The interior of the aircraft is sprayed with a pyrethrin freon aerosol containing not less than 0.4 per cent. pyrethrin, or containing not less than 0.4 per cent. pyrethrin and 3 per cent. DDT, applied from an aerosol dispenser for a period of not less than 15 seconds per 1000 cubic feet of free air space. All openings in the aircraft are kept tightly closed during the spraying and for a period of five minutes thereafter.

When disinsectization has been carried out as described, a certificate to this effect issued by the Quarantine Office of the Ministry of Health, at an airport in this country will be accepted by the Indian Government as proof of adequate protection for the particular aircraft.

In the case of yellow fever the Indian Government considers that an aircraft is "suspect" if it arrives in India from the West, and "infected" if (a) it has a case of yellow fever on board; (b) it has on board a non-immunized person who has been in a yellow fever area within nine days; (c) if either of the above conditions apply and the aircraft has not been disinsectized, in accordance with the prescribed method.

Regulations applying to the other diseases mentioned are described in detail in the regulations of the International Sanitary Convention. Confirmation that the measures required have been adequately carried out has to be presented to the authorities by the captain of the aircraft in a form of certificate which is similar to the declaration of health at present in use for shipping.

AIRCRAFT WATER SUPPLIES

Water is a frequent conveyer of disease, and it is therefore essential that a standardized routine should be adopted for the sanitary protection of supplies from source to consumer. Sufficient quantities to last throughout the round flight of an aircraft cannot be carried in the tanks, and airlines are therefore faced with the problem of local overseas sources and the maintenance of the necessary quality to ensure safety. This involves in-

cessant watchfulness over the cleansing of aircraft tanks, delivery bowzers, hosepipes, and portable containers, and chemical treatment in the aircraft itself of all water drawn off for consumption during flight. This is achieved by removing all water tanks from aircraft at servicing bases at home for manual scouring and steaming, followed by strong chlorination of the cleansed interior before filling with fresh potable water before initial take-off. As an additional precaution all water taken on at staging posts overseas should be charged during flight with some recognized sterilizing agent, such as chloramine-T or halazone, before it is served, either for direct consumption or for making soft drinks. In addition, all vacuum flasks containing water and food should be boiled after return to base, and again before being refilled with fresh supplies for a subsequent flight.

Samples of water remaining in the tanks of aircraft arriving in the United Kingdom from abroad should be taken regularly and submitted to bacteriological examination. A system of constant supervision should be established, and there should always be close liaison with the local Port Health and Sanitary Authorities.

CONCLUSIONS

The speed of air transport has resulted in the institution of what, at first sight, might appear to be unnecessarily stringent and cumbersome regulations, but with the possibility of passengers and aircraft being in an endemic and non-endemic area on the same day, it is impossible to ignore the results which relaxation of such health measures might bring about, and until there is more effective control of pestilential disease such restrictions will continue. One suggestion which has been made is that airports which are largely used in transit might be strictly controlled so that all personnel working in them would be immunized, the area itself completely epidemic free, and the buildings made to conform to stringent regulations in order to eliminate the risk of infection of passengers in transit. It should also be noted that epidemiological conditions throughout the world are constantly changing, and emergencies arise with little or no warning, so that regulations which are in force to-day may be changed to-morrow. It is therefore always wise to consult reputable publications or a recognized authority on the matter before embarking on an air journey overseas, in order to ensure that the current regulations are being complied with. Non-compliance may result in embarrassing or irritating delays in other countries which could have been avoided by attention to such details.

All are agreed that a reduction in controls and certificates is desirable, but until such time as it can be ensured that such relaxation will not result in transmission of disease from endemic to non-endemic areas, such a step would be unwise. Travellers by air may be assured that responsible authorities will only take such measures as are necessary in the interest of safety.

STANDARDS OF FITNESS FOR CIVILIAN FLYING CREWS

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No one doubts the importance of insisting upon a high standard of physical efficiency for the crews of commercial aeroplanes, nor that, if airlines are to be made to pay, accidents must be reduced to a minimum. Maintenance of the physical efficiency of the operational staff is one of the most important factors in ensuring an accident-free service.

INTERNATIONAL STANDARDS

Before the war the medical requirements for civilian flying crews were based on agreements which were thrashed out at a number of meetings of an International Convention for Air Navigation (I.C.A.N.). The whole field of civil flying was surveyed at these meetings, and drawing up medical standards formed only a small part of the work. The most recent meeting of the Medical Committee of I.C.A.N. was held in Paris soon after the liberation, when the medical standards drawn up at previous conferences were reviewed in the light of experience gained during the war. The principal recommendation then adopted was that an X-ray of the chest should be taken at the first examination of every candidate for a civil flying licence. Delegates from only seven nations sat on this Committee so that there were some notable absentees, although the U.S.A. and Canada were represented by non-medical observers. It is easier to criticize regulations such as these than to draw them up but, making every allowance, there can be no doubt that the medical requirements for civil flying as detailed by the I.C.A.N. left much to be desired. They were written in a stilted language often using medical terms not in general use; on some matters they were far too rigid, on other subjects of great importance they maintained a discreet silence.

Since the war, a new body has been formed called the International Civil Aviation Organization, and at the first meeting the question of medical requirements came up for discussion. The suggestion was adopted that these should be divided under four headings:—

- (1) Physical requirements
- (2) Visual requirements
- (3) Colour perception requirements
- (4) Auditory requirements

There are to be three grades of physical requirements, three grades of visual requirements, two grades of colour perception requirements, and four grades of auditory requirements. By combinations of the various

gradings the appropriate standards for each member of the crew of a commercial aeroplane, pilot, flight radio operator, flight engineer, and navigator, have been drawn up. Thus the flight radio operator will require a high standard of hearing but his vision can be of a comparatively low grade; the flight engineer's visual and auditory requirements need not reach the highest grades.

The visual and auditory requirements need not worry us here, for it is solely with the physical fitness that we are concerned. The new recommendations envisage a high standard of physical fitness for the pilot of an airliner, who must be of No. 1 physical grade, and for the pilots of freight carrying aeroplanes and all members of aircrew, who must be of No. 1 or No. 2 physical grade. In actual practice, whilst the visual and auditory standards do vary considerably, physical grades No. 1 and No. 2 differ hardly at all. No. 3 physical grade is distinctly lower and applies principally to pilots of private aircraft, flying their own machines for business or pleasure.

As is usual in international conferences there was a good deal of disagreement, and again there were some notable absentees, although on this occasion the U.S.A. was fully represented. As yet no country has issued any regulations based on these new recommendations, so that the I.C.A.N. agreements still stand.

FLYING PERSONNEL

Individuals applying for licences to fly in an aeroplane "flying for hire and reward" can be classified into three groups:—(1) Pilots and aircrew of the Airway Corporations flying big machines over long distances; (2) pilots and aircrew of the private Charter Companies usually flying smaller machines; (3) a miscellaneous group consisting of flying instructors, test pilots, and the like.

The remarks which follow apply more directly to the first of these groups, the men who fly the big airliners, although they do apply to a great extent also to the members of the other groups. With this as a background one can now proceed to discuss one's own opinions as to the standards of physical fitness for civilian flying crews. The subject is a big one, and in a short article it is possible to mention only certain points. The problem may be considered under two headings:—(1) Physical requirements for candidates for training as civilian flying crews, and (2) physical requirements for trained personnel.

PHYSICAL REQUIREMENTS FOR CANDIDATES FOR TRAINING AS CIVILIAN FLYING CREW

Up to the present British Airlines have recruited a majority of their staff

from personnel of the Royal Air Force who have completed their term of service; an economical measure and one that seems likely to continue to the benefit of both Service and Civil Flying. In general, the medical standards of the R.A.F. correspond to the standards required of the civilian pilot or member of aircrew. This fact, however, does not mean that the medical examination on transfer from Service to Civil Flying should be omitted or lightly undertaken. At least five years will have elapsed since the original examination for fitness for flying training and, although the candidate at the time of transfer will be fit for all flying duties, evidence may have accumulated during the period of service which suggests that all is not well for the future.

At this point a difficulty arises. The Licensing Authority is confined to an expression of opinion as to fitness for flying during the period for which the licence is valid; six months for a pilot and a year for a member of an aircrew. A candidate who is fit at the time of medical examination, and is likely to remain so during the licensing period, may not be assessed as unfit by the Licensing Authority on the grounds of probable unfitness at some time in the future. It is, of course, possible that the candidate intends to complete only a few months' flying before taking up a ground appointment. If the candidate is passed fit and accepted, the Airline Corporation will have to spend a good deal of money in further training, and will hope in return for many years of service free from illness. In most cases what they require is a long-term assessment of the health prospects of the candidate. The doctor cannot be expected to be a prophet, but there are certain points in the history and in the examination of a young adult which indicate that the flying life is not likely to be a long one, or will be interrupted at intervals by ill-health. The work to be done is strenuous and tiring and among other things involves the most rapid changes of climatic conditions. The interests of all concerned will best be served, at this stage, by insisting on the highest grade of physical efficiency, and attempting to eliminate those likely to break down sooner or later during their flying career.

GENERAL MEDICAL EXAMINATION

This follows the usual lines and it is unnecessary to go into details, but one or two points may be considered. A carefully taken history is essential; it is not enough to hand the candidate a series of questions and allow him to fill up the answers without further comment. Leaving aside for the moment the question of flying there are certain diseases which fare badly in tropical climates, and any history of these conditions calls for special questioning. Foremost must be put *skin diseases*, which form the chief cause of disablement in hot climates. Any tendency to eczematous or seborrhœic states should be a bar to acceptance. Some skin conditions, such as psoriasis, are said to do well in the tropics, but this is by no means always the case, and a

candidate with any form of skin lesion should be viewed with considerable disfavour.

Second only to skin disease as a cause of disability in the tropics comes *bronchitis*, and a history of winter coughs or any tendency to chest trouble should be a cause for rejection. It is sincerely to be hoped that the late war has exploded once and for all the theory that all tropical or subtropical climates are good for bronchitis.

Similarly, a history of *pleurisy* with effusion should be a bar to acceptance. A follow-up of cases occurring in the Services during the war showed that, even with treatment along sanatorium lines for a period up to six months, about one in four subsequently developed pulmonary tuberculosis. Another potent cause of disability among young adults is *indigestion*, and airline flying, involving as it does irregular and often hastily eaten meals, can only aggravate any tendency this way.

A history of *fainting attacks*, or of attacks of giddiness or dizziness, should be carefully inquired into, for the candidate is likely to gloss over this question as he probably knows the importance that will be placed upon it. Any history of recurrent fainting attacks, even though obviously cardiovascular in origin, should lead to rejection.

ANCILLARY EXAMINATIONS

Chest X-ray.—Every candidate should have a skiagram taken of his chest and any abnormality found should be investigated. A lesion which is presumably tuberculous in origin, if it is not completely calcified, should be regarded with suspicion. Flying, with its sudden alteration in intra-pulmonary pressure and variations in pulmonary ventilation, is not good for the tuberculous patient, and at this stage rejection is the best course.

Electrocardiogram.—The routine electrocardiogram is not so valuable as the routine X-ray of the chest, but some Civil Aviation Authorities insist upon one being done, and every now and again an unexpected result occurs. It is worth doing if the facilities permit.

Electro-encephalogram.—The routine electro-encephalogram is even more difficult to defend, although Williams (1947) has stated that it might eliminate half the potential epileptics. When only comparatively small numbers are involved the labour would not be great and it would be an added safeguard.

Quite apart from any immediate gain from these three examinations the records form a base-line by means of which subsequent examinations may be judged, and on these grounds alone have proved their value.

Many other examinations have been recommended at one time or another, in particular a routine Wassermann reaction. A case might equally be made for a routine blood count, intravenous pyelogram, or even a routine ventriculogram, but common sense must call a halt and own that the only

really essential examination besides a full clinical examination is the chest X-ray.

CLINICAL OBSERVATIONS AND PHYSICAL EFFICIENCY TESTS

At the first examination a few clinical observations which can be measured or graded with fair accuracy should be done and the results recorded; at the same time one or more simple physical efficiency tests should be performed.

(1) *Weight and body build.*—Any marked deviation from the normal body build is an adverse characteristic. Although there are many instances of both overweight and underweight individuals who have led healthy, active lives, there is evidence that over a period of years both groups are more liable to illness than are those of normal build.

(2) *Pulse rate.*—At the first and possibly at one or two subsequent examinations the candidate may be under considerable stress, which affects the results obtained; an emotional tachycardia is often found, the pulse rate keeping persistently about 96 a minute or even higher. Nervousness at the early examinations does not betoken a lessened chance of becoming a successful pilot. If these individuals are kept under observation it will nearly always be found that the tachycardia and similar accompaniments have disappeared by the time the early days of training have passed.

(3) *Blood pressure.*—The blood pressure is often affected by the nervous tension of the first examinations. Both systolic and diastolic pressures may be raised, the systolic more than the diastolic; it is quite common at the first examination to find a systolic level of 150 mm. of mercury or even higher. If a little time is taken to gain the confidence of the candidate it will often be found that the blood pressure settles down to a lower level. The diastolic pressure in a man below the age of twenty-five years should be between 70 and 85 mm. of mercury. There is evidence that with a level persistently above 85 mm. of mercury at this age, hypertension in the thirties is more likely than in individuals with a diastolic pressure below this level. A diastolic pressure which is persistently below 70 mm. of mercury is often associated with a tendency to attacks of syncope. Candidates with diastolic pressure above or below the levels indicated are best rejected.

(4) *Tremors.*—These are judged with the candidate standing with the arms held straight out at shoulder level and the fingers extended and spread out, and are recorded as fine or coarse, slight or marked.

(6) *Physical efficiency tests.*—Many different forms of physical efficiency tests have been advocated at one time or other, with a general tendency to become more and more complicated. The type of test selected should vary with the strain that the individual is being asked to withstand, and as the physical strain involved in piloting or in aircrew work is comparatively slight, strenuous tests are here out of place. For flying personnel the tests chosen should be simple, easy to carry out with the minimum of apparatus,

should not consume too much time, and the "end point" should be sharp and distinct. After thirty years' experience with certain tests, their fallacies and their failings as well as their strong points become familiar, and one may perhaps be pardoned for being prejudiced in their favour. Hence if two tests used in the R.A.F. are recommended it does not imply that they are necessarily the best or that others are of no value. The first test is an exercise tolerance test with measurement of the pulse rate before, immediately after, and at a stated period after the test exercise. The second test is Martin Flack's "endurance test", in which a column of mercury in a U tube is blown up to a height of 40 mm. and then held at that position for as long as possible while the pulse rate at the wrist is taken at 5-second intervals.

ASSESSMENT

The candidate for flying duties should have a good family history, a past history free from serious disease, and no evidence of any disability on routine clinical examination. Due allowance must be made if the clinical observations and physical efficiency tests do not reach the highest standards at the first examination. The usual course of events when carrying out these observations and tests is that after the first one or two trials there is improvement in the results, which settle down to a steady level, and at this level they remain with little variation so long as the individual keeps fit. Should some illness result, or should slackness as regards health occur, with too little regard for sleep and open-air exercise, and too much indulgence in alcohol and smoking, it is surprising how often this is revealed in the tests. The pulse rate begins to rise, the blood pressure to increase, the tolerance to exercise is not so good, the mercury is not held up so long, and the pulse responses are not so steady. There is no doubt that routine observations and tests form the best, if not the sole, method of keeping a check on the physical fitness of a number of young men. The criticism is often heard that so and so is "beating it up", yet the results of his physical efficiency examination show no deterioration. This may be true but is simply further evidence of the strength and adaptability of the human frame. Moreover, as in most medical tests a fair degree of loss of efficiency has to occur before it becomes apparent in the results, when it does occur there is all the more need to take it seriously.

One of the fallacies of physical efficiency tests is that motivation plays a considerable part in the results obtained. When the candidate is a free agent and obviously wants to do his best this factor does not enter, but when a sudden deterioration in performance has occurred, before concluding that ill-health is necessarily the cause, it is wise to inquire into the psychological aspects of the case. There is much to be said, despite obvious drawbacks, for a Physical Efficiency Index, such as the Flack Index or the American Schneider Index, in which a figure is given at each medical examination

as a guide to the degree of fitness of each individual. A warning that his Physical Efficiency Index is falling, with the possibility that further fall may result in the loss of his licence, has often pulled a man up short and has resulted in his living a quieter and more sober life, to the benefit of his health and of his flying.

MEDICAL REQUIREMENTS FOR TRAINED FLYING PERSONNEL

In accordance with the regulations the medical examination for renewal of the pilot's licence has to be repeated at six-monthly intervals throughout the individual's flying career; for aircrew the medical examinations are repeated at yearly intervals. A certificate is signed by the applicant stating the amount of flying done since the last examination and whether he has been off flying duty as the result of illness or accident. The examination follows the same general lines as that done on entry, the clinical observations and physical efficiency tests are repeated and the results compared with those of previous examinations. Ideally, the X-ray of the chest should be repeated at each examination, but the electrocardiogram and electro-encephalogram are done only if there is some clinical indication. Any deterioration in the results of the tests calls for special care in the examination; if deterioration is marked, yet no cause can be found, the licence should be withheld and the applicant examined again after a short period. If there is no improvement the applicant should be referred to his doctor for investigation.

The medical standards for trained pilots and aircrew should not be so rigid as for the candidate for civil airline work. Within limits, flying experience makes up for medical disability, and although high standards must be maintained the doctor should be allowed some discretion. Without this liberty of action there will inevitably be a serious wastage of highly skilled personnel; the doctor should have the power, when he feels it is necessary, to limit the strain thrown on an individual and not simply the power to stop flying altogether.

Limitation of flying.—The method of limiting flying, used so successfully for many years in the R.A.F., has no real counterpart in civil flying. In the R.A.F. it is possible to limit the duration of flying time, either of individual flights or the number of hours flying to be done in a day, to limit the height, or to limit flying altogether unless a co-pilot is carried. In the civil airlines, flying on scheduled routes, it is a method that might be difficult to apply, but without some such plan pilots and aircrew are often condemned to unnecessary periods of inactivity which are uneconomical for the employer and bad for the employee. To carry out the scheme effectively it would probably be necessary for the various airlines to be integrated so that pilots and aircrew could be switched from the longer to the shorter routes. One might hesitate before passing a pilot as fit to fly to Australia but would have no hesitation in allowing him to fly from London to Manchester, so long as adequate rests between flights could be taken. The most valuable

limitation would probably be that of flying with another pilot, for most airliners carry two pilots, and it would be comparatively easy to implement. If it is certain that someone else could take over should the need arise, there are many instances when return to flying could be allowed, whereas to permit flying as the sole pilot would be quite unjustifiable. This limitation can, of course, only be permitted when the doctor is as certain as it is possible to be in medical matters that symptoms will not recur, but regards a practical test as the best form of assurance.

MEDICAL DISABILITIES

It is impossible within the limits of a short article to discuss all the medical conditions that may cause difficulties, but two of the common ones will be touched upon.

Pulmonary tuberculosis.—The routine X-ray of the chest has raised almost as many problems in aviation medicine as it has solved. In the case of active disease no question arises; treatment is required, and all flying must be forbidden for some long period. It is the lesion of doubtful activity which leads to so much difficulty. If the standards and methods of examination which have been suggested are adopted, any lesion found on routine X-ray must be of recent origin. It would thus be necessary for the patient to submit to medical observation to ascertain if general symptoms were being caused, or if tubercle bacilli were present in the sputum or gastric washings. If after a year's observation the lesion is small and apparently healing, return could be allowed to limited flying, the limitation being as regards height (not above 5000 feet) and duration (flights of not more than three hours). If a routine three-monthly X-ray shows no extension of the lesion these limitations can gradually be extended in favourable cases until a flying category, limited to temperate climates only, is allowed after two years' observation. After a further year's observation full flying could be resumed. The exact duration of the different stages is varied according to the clinical condition of the patient and the X-ray findings, but should rarely be less than those indicated, and might well be more.

Patients with hæmoptysis or pleural effusion, presumably of tuberculous origin, should be dealt with on similar lines.

Peptic ulcer.—Most clinicians are agreed that worry and acute emotional episodes have a more or less direct effect in the causation of peptic ulceration. If this is so it should be possible to show that flying, particularly war-time flying, causes an increase. In the R.A.F. during the war there was a general increase in the incidence of peptic ulcer among flying and ground staff, both officers and men; the increased incidence among the ground staff was a little over one-and-a-half times as great as in peace time; in the flying branch it was over three times as great. There are, however, so many factors to be taken into account that caution is necessary before accepting the greater incidence as being due to increased nervous tension.

Flying an airliner to schedule often necessitates hasty and irregular meals, whilst the quality and cooking of the food obtained on the journey often leave much to be desired. Particularly in the case of the younger men there is a lack of knowledge of how to look after themselves in a tropical climate, and gastro-intestinal upsets are common complaints. In uncomplicated cases, when the diagnosis of peptic ulcer is confirmed by the X-rays or the symptoms are so typical that the diagnosis seems certain, the patient should be warned that he must undergo a full course of treatment, and that he is unlikely to obtain a renewal of his licence for several months. If after treatment he has been free from symptoms for six months he can be allowed to make short flights. After a year's freedom from symptoms the flying time can be extended, so long as there is a reasonable prospect that regular and good meals can be obtained; flying in tropical countries should be forbidden until at least two years of complete freedom from symptoms have elapsed. Bleeding from a peptic ulcer is a not uncommon cause of syncope, and often there are few symptoms beforehand to give a warning. There is a tendency for the same complication to occur in subsequent attacks; hence even greater care is necessary before permitting return to flying.

It has recently been shown that the prognosis after perforation of an ulcer is not so good as was thought at one time, for there is a high incidence of recurrence of symptoms and of further complications. In these patients, too, extreme caution is essential, and sometimes permanent removal from flying is the only course.

CONCLUSION

A recommendation of permanent withdrawal of the flying licence on medical grounds, although sometimes inevitable, is a step which the doctor always seeks to avoid. It is often possible, given the opportunity, to nurse a pilot or member of an aircrew whose health has broken down, back to the standards of fitness required for the most strenuous flying duties.

The difficulties in laying down regulations governing the medical standards for civilian flying are enormous, for so many varying factors have to be taken into account. Strict and rigid standards must be set for the selection of the untrained, but if these same standards are made to apply to the trained there will inevitably be a serious wastage of valuable personnel. Some liberty of action should be allowed to the doctor in assessing the fitness of trained pilots and aircrew to return to flying. Whether or not this liberty will be permitted has yet to be decided, and how it can be transcribed into regulations which will satisfy an International Convention has yet to be worked out.

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MOTION SICKNESS: WITH SPECIAL REFERENCE TO AIR SICKNESS

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MOTION sickness consists of a well-defined series of symptoms experienced by susceptible individuals on exposure to various types of motion. The symptoms are essentially the same whether the motion is caused by the movements of an aircraft, boat, motor vehicle, train, swing or devices in amusement parks, and it is likely that the causative mechanism is identical. Individual susceptibility to motion sickness varies greatly, but most persons typically show a marked ability to become adapted to any particular form of motion. It is probable that no one would be immune to the condition if exposed to violent enough motion continued for a sufficient length of time. Although sea sickness has been a problem for centuries the history of the study of air sickness dates from the war of 1914, when a few attempts were made to pre-select and eliminate air-sick individuals from flying duties. Since 1939, the problem has been studied extensively, and knowledge of the etiology and treatment of the condition has been greatly advanced.

Symptoms.—Although the symptoms of motion sickness may vary greatly in degree with different individuals the typical chain of events is as follows:—Transitory exhilaration followed by uneasiness, drowsiness, yawning, pallor, epigastric awareness, malaise, cold sweating, nausea and vomiting; salivation, headache and increased peristalsis of bowel occur less frequently. A continuation of the exposure to motion leads to repeated nausea and vomiting, fatigue, mental depression, and interference with general efficiency.

Incidence.—The frequency of air sickness is difficult to assess since such factors as previous flying experience and weather conditions are influencing factors of major importance. Observations made on Royal Canadian Air Force trainees showed that of 2,682 aircrew, 15 per cent. were ill at least once, and 0.5 per cent. were forced to discontinue training (Mathewson, 1942). In 3,526 four-hour flights the incidence of sickness was high, up to 60 per cent., especially in persons inexperienced in flying. The incidence of motion sickness in pilots of aircraft is extremely low, even though they may become airsick when travelling as passengers (Armstrong, 1943). An individual showing symptoms of illness will rapidly return to normal should he take over control of the aircraft.

ETIOLOGY

Numerous causes of motion sickness have been suggested and the subject has been reviewed by McEachern, Morton and Lehman (1942). The most

conclusive evidence indicates that stimulation of the labyrinth is the cause of motion sickness. Recent experimental work has confirmed the original observations of Sjöberg (1931) that destruction of the labyrinth renders previously susceptible dogs immune to motion sickness. Similarly, humans with absence of vestibular function are also immune. Whether the semi-circular canals or the utricle is the organ primarily affected is not certain, although most evidence favours the latter (McNally and Stuart, 1942; Howlett and Brett, 1943). A number of observations have been made on humans exposed to motion on swings, and the importance of the position of the head in relation to the direction of motion has been emphasized (Howlett, Wardle and Brett, 1943; Stewart *et al.*, 1943). If the line from the external auditory meatus to the lateral canthus of the eye is at right angles to the arc of the swing the incidence of illness is low. When this line is parallel to that of the swing the incidence is high. Lying prone on the back with the head flat, or sitting with the head thrown far back are therefore positions in which the effect of motion is minimal. On the other hand, lying on the back with the head bent forward, or the ordinary sitting position, are both associated with a high incidence of sickness. Head positions which allow the greatest stimulation of the utricle are therefore associated with the greatest effects of motion and point to this organ as the chief cause of the disturbance (Howlett and Brett, 1943). Visual, auditory, gustatory and olfactory sensations, as well as psychological factors, may be augmenting causes in certain cases.

Types of effective motion.—Various types of motion have been used to induce vomiting in man and animals. Special machines which imparted a sideways and vertical motion were not found to be more effective than a simple swing. When the component motions of a swing are tested separately it has been found in man (Manning, 1943a; Fraser and Manning, 1943) and dogs (Noble, 1945a) that the vertical motion is relatively ineffective, and angular movement of no effect, when used at the same frequency and magnitude as in a swing. Extreme changes in vertical acceleration as induced by elevators may be quite effective stimuli. Changes in horizontal acceleration seem to be the most effective in inducing sickness, although no single component movement of the swing is as effective as the composite motion. The frequency of the change in acceleration would seem to be of importance as well as the over-all alterations in "g", since slow or rapid swinging actions are less effective than a moderate one. Reduction of "g" in a swing, by diminishing the angle and length of arc of swinging, markedly lowers the production of motion sickness.

During the training of Service personnel it was hoped that by preliminary testing on swings it might be possible to pick out individuals who would later become airsick. Extensive observations, however, have shown that there is not necessarily a close parallelism between air and swing sickness (Brown, Brett and Howlett, 1943; Stewart, Manning and Suther-

land, 1943). In general, however, it may be stated that a person with a poor history of motion sickness or who reacts strongly and rapidly to swinging is likely to become airsick. The swing apparently is a powerful stimulus, since nearly everyone who experiences air or sea sickness will be sick on swinging. On the other hand, many who become sick on the swings do not do so with other types of motion.

ADAPTATION

Most individuals accustom themselves rapidly to any form of motion and so become immune. Probably less than 1 per cent. cannot adapt themselves in a reasonable length of time, so that the number of persons who cannot work on ships or aircraft is small. Adaptation to motion has an extraordinary feature in that it is apparently highly specific for only one particular type of movement. Persons adapted to motion on swings are not similarly immune in aircraft (Manning, 1943a; Gibson, Manning and Cohen, 1943). Likewise, sailors changing from one class of vessel to another have to become re-adapted to the change in motion. Adaptation to motion in dogs takes place in the usual manner, even if the animal is protected from motion sickness by suitable drug treatment.

EXPERIMENTAL MOTION SICKNESS IN ANIMALS

Susceptibility.—Swings have been employed to produce vomiting in dogs and cats, and susceptible animals have been extensively used for the testing of motion sickness remedies. Cats are considerably less susceptible than dogs, about 15 per cent. vomiting when swung through an angle of 90° on a swing with a $14\frac{1}{2}$ ft. radius. Only an occasional animal may be made ill repeatedly with a consistent response. Dogs, on the other hand, under similar conditions are highly susceptible, and of 70 animals tested 81.5 per cent. vomited within forty-five minutes after the start of the swing (Noble, 1945a). By reducing the angle of swinging and hence the stimuli exerted by changes in gravity it is possible to determine the degree of susceptibility and to classify different dogs accordingly. Animals of moderate or high susceptibility show a good consistency in their response to motion when used at weekly intervals over a period of years.

In one case an animal was swung on 148 occasions during a period of three years and vomited 117 times. On 67 tests this animal received either no treatment or treatment with inactive drugs, and the time of vomiting was 13 ± 4.5 minutes (Noble, 1945b).

In these experiments no evidence of conditioning was observed, so that reflex vomiting at the sight of the swing is not a factor in the results. Adaptation to the swing which renders the dog immune may occur in animals of low susceptibility or when any animal is swung repeatedly at intervals of less than five days.

A group of 16 dogs which were susceptible to swing sickness was exposed to

rough weather conditions in an open boat. In a short interval 7 of them had become seasick and, in addition, 4 other dogs became car-sick while being transported to the lake. The animals which were the most susceptible on the swings were not necessarily those which became ill in the car and boat; a finding comparable to the experience described in humans.

TREATMENT

In 1942, when a search was started for drugs which might prove effective against motion sickness, it seemed possible that certain barbiturates might possess a specific depressant action on the higher centres concerned with vomiting. The problem was to find such a substance which would have this specific effect and yet not show any undesired side-actions, such as inducing hypnosis (Noble, 1945b). Many reports in the literature indicated that sedation following treatment with amytal, nembutal, or phenobarbitone was a beneficial form of therapy (Hamilton, 1932; McLaughlin, 1935; Hill, 1936). The use of such hypnotic compounds, however, was undesirable in Service personnel. From the early results obtained on dogs it was apparent that many barbituric acid derivatives possessed the property of preventing motion sickness and that this action was not related to their hypnotic or anæsthetic property. A compound such as ethyl- β -methylallyl thiobarbituric acid* (designated V-12) prevented vomiting in all dogs in oral doses of from 1.25 to 30 mgm./kgm., depending upon the susceptibility of the animal. Such a compound has little hypnotic action and in the therapeutic dose-range used does not give rise to any demonstrable side-effects. This substance was used as a standard for comparing other compounds. Of some 175 barbiturates tested, a few were found to be considerably more active than V-12, but subsequent toxicity tests precluded their use in humans.

Drugs other than barbiturates have been tested on dogs, and bromides and bulbocapnine have been described as being of benefit (Babkin, Dworkin and Schachter, 1946). The belladonna alkaloids which are effective in humans do not possess any protective action against motion sickness in dogs (Babkin and Dworkin, 1942; Noble, 1946).

Therapeutic tests in humans.—When the necessity of transporting troops by air and sea for the invasion of Europe became apparent, large-scale testing of motion sickness remedies was undertaken by groups of workers in England, the United States, and Canada. A comprehensive review of such studies has been published recently (Noble, Sellers and Best, 1947).

Initial experiments consisted of testing humans on swings and attempting to evaluate therapy before beginning sea trials. After testing 3,415 naval ratings on swings it was found that 35 per cent. vomited within half an hour. Using swings of slightly larger dimensions, 56.6 per cent. of a group of 369 individuals vomited (Noble, 1946). Repeated tests on susceptible persons showed that approximately 85 per cent. vomited repeatedly and that the time of vomiting was within ± 13 minutes of the initial test. In 54 per cent. of cases the time of vomiting on the swing was within ± 4 minutes on two successive tests.

* Supplied by Abbott Laboratories, Chicago.

Drugs.—Of the various preparations tested against motion sickness, *hyoscine hydrobromide* and a mixture of *hyoscine hydrobromide* and *hyoscyamine hydrobromide* were the most active, protecting from 40 to 75 per cent. of susceptible persons. *Hyoscine hydrobromide* alone in doses of 0.65 to 0.8 mgm., given orally an hour or two before swinging, was probably not as well tolerated or quite as effective as a mixture of *hyoscine hydrobromide*, 0.3 mgm., and *hyoscyamine hydrobromide*, 0.8 mgm. *Atropine* was less effective. Various *barbiturates* were tested in swing experiments and V-12 was used most extensively. A total dose of 5 grains (0.32 gm., usually divided and taken morning and evening with food) gave as good protection as large doses of *hyoscine*. V-12 and *hyoscine* combined showed slightly improved effectiveness.

A number of sea trials was conducted with the above and other compounds. In English trials *hyoscine* was shown to be highly effective, some 50 to 70 per cent. of susceptibles being protected (Holling, McArdle and Trotter, 1944). In tests in California the protective action of *hyoscine* was confirmed and mixtures of *hyoscine* and *hyoscyamine*, as given above, or *hyoscine hydrobromide*, 0.4 mgm., *atropine sulphate*, 0.3 mgm., and *sodium amytal*, 130 mgm. (motion sickness preventative M.S.P.—American Army development type), were all equally effective, giving approximately 40 per cent. protection over a placebo. V-12, given as a single dose of 3 to 5 grains (0.2 to 0.32 gm.), was found to be almost as effective. Unreported tests have since indicated that the most effective form of therapy with V-12 alone is to give continuous dosage of $2\frac{1}{2}$ grains (0.16 gm.), a.m. and p.m., beginning a day before exposure to motion. Only brief reports have been made on the value of these drugs in air sickness, *hyoscine* and M.S.P. being stated as of no effect or of affording some protection (see review by Noble, Sellers and Best, 1947).

In evaluating the effects of treatment it is important to remember that *psychological factors* may contribute to motion sickness and that any form of therapy may have a favourable effect. In the various sea trials conducted, placebo capsules of lactose were found to reduce the incidence of sickness in as many as 20 per cent. of cases, depending upon the severity of motion. Specific forms of therapy therefore, to be of value, have to allow greater protection than that afforded by the administration of a placebo.

As a result of the Canadian studies the following mixture termed the "Canadian Motion Sickness Remedy", National Research Council Formula, has been recommended for further trial in motion sickness:—

<i>Hyoscine hydrobromide</i>	0.1 mgm.
<i>Hyoscyamine hydrobromide</i>	0.3 mgm.
Ethyl- β -methylallyl thiobarbituric acid (V-12)	130 mgm.

The suggested dose for an adult is 2 capsules taken two to four hours before exposure to motion, with a further treatment of 1 capsule every eight to twelve hours, but in no case should more than 3 capsules be taken in twenty-four hours. Increased benefit may be obtained by starting therapy the day before exposure. If *hyoscine hydrobromide* is used alone, a single dose of 0.65 mgm. is usually well tolerated. With V-12 alone, divided doses of $2\frac{1}{2}$ grains (0.16 gm.) twice daily, taken with meals, are not likely to cause

sleepiness or other side-effects. It should be noted, however, that since V-12 is a barbiturate containing sulphur and is related to diethyl thiobarbituric acid there is a potential danger of causing agranulocytosis. Toxicity studies in which 5 grains (0.32 gm.) of V-12 have been taken daily for a month have not shown any toxic action on liver or bone marrow. When therapy is required for long periods it is recommended that the drug be given only on five days of every seven, so that cumulative effects may be prevented.

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MEDICAL CONTRAINDICATIONS TO FLYING

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LONG-DISTANCE air travel has now been an accomplished fact for more than a quarter of a century, yet there are still those to whom it is something sinister and who doubt their fitness to endure it. At the other extreme there are enthusiasts among both doctors and patients who see in the quick transportation which air travel can provide the answer to nearly every medical and surgical problem which may arise in localities remote from specialist help. In fact, there is nothing in air travel which need in any way prevent an ordinary healthy being from using this means of getting about. On the other hand, in any journey by air there are factors which, if they become operative, may have definite physical effects on human beings. For people in average health these effects may mean the difference between a comfortable journey and one which is uncomfortable or even distressing. For people whose health is below average or who are patients, the summation of effects may be serious and may even threaten life. In any doubtful case it would be possible to investigate an individual's tolerance of some of the factors by means of the experimental decompression chamber. It will be well to discuss these factors and their potential effects as a background to the more strictly medical contraindications to flying.

GENERAL AND PERSONAL CONSIDERATIONS

Bumpiness (the sudden rise or fall of the aircraft in association with atmospheric changes). Passenger air travel does not involve aerobatics, and in the ordinary way the route is chosen for a given flight so as to avoid encountering serious weather disturbances. The pilot will have been briefed and given his flight plan, and he cannot be expected to make any departures from this or to give any guarantee to fly below a certain altitude. The evolution of larger aircraft and various modifications in design have both tended to reduce the effects of weather disturbances and to lessen bumpiness, but the latter remains a factor which must be taken into consideration.

Noise.—According to the design of the aircraft and the effectiveness of insulation, this may vary from a low hum to an intensity which makes any verbal communication other than by shouting an impossibility. Many people believe that it is noise which makes air travel so exhausting. Certainly for a patient it might on occasion be a grave disadvantage.

With increase in *altitude* go decrease in *temperature*, decrease in partial

pressure of oxygen, and reduced total atmospheric pressure and density of air. Each of these factors is, to some extent, capable of modification. The effects of temperature reduction can be offset by adequate warming, either by special clothing or electrical heating apparatus. Oxygen can be administered to individual passengers (although there are certain difficulties in the case of infants), or the whole passenger cabin can be air-conditioned and "pressurized". If oxygenation and body temperature are not maintained, then slowing of intellectual and bodily functions will follow in the normal individual. In a patient the effects might be serious and appear at a level much below that which obtains in health. In contrast to the effects of reduction of temperature and of partial pressure of oxygen, pressure *per se* up to sixteen atmospheres (500 ft. sea depth) or down to one-seventh of an atmosphere (45,000 ft. altitude) is without primary effect on tissues. It is the failure of sufficiently rapid attainment of equilibrium between such pressures and those of body cavities, or the production of changes in volume of body gases, which are the important factors. The reduction in pressure for equivalent elevations is greatest near the earth and becomes progressively less during ascent. Thus, the change of pressure from 5000 to 6000 ft. is 23.3 mm. of mercury, whereas from 15,000 to 16,000 ft. the change is 17 mm. of mercury, and from 35,000 to 36,000 ft. 8.3 mm. of mercury.

The consequences of these pressure changes may be of considerable importance in cases in which it is not possible to explain to an individual traveller what is happening and what should be done to compensate. Thus, the pressure effects in the ears may be serious in infants or young children, who should always be fed on descent in order to ensure opening of the Eustachian tubes. Similar considerations apply in the case of mental defectives or people of poor understanding who may become alarmed and agitated at the strangeness of certain bodily sensations. Gaseous distension of the gut is experienced by certain individuals at altitudes of 5000 ft. and over, and of itself the distension may constitute a drawback to air travel in subjects of ulcerative conditions of the gastro-intestinal tract. Active ulceration or complications such as hæmorrhage or perforation are contraindications to flying within six weeks of their happening. People with a colostomy opening must be prepared to deal with irregularities in its action.

If there is genuine *fear of flying*, and an individual is likely to spend the whole trip in a state of more or less misery, holding tightly on to the arms of his seat, then he had better not travel by air. There is no compulsion upon anyone to fly, but if the question does arise in connexion with work or a business appointment then it would be better to face up to the situation as a temperamental or psychological problem, and as a matter affecting the working conditions of an employee. The possession of a *nervous temperament* or disposition is certainly a liability in air travel. Such people may be expected to show, in an exaggerated form, the effects of apprehension normally experienced in a first flight. There may be lack of emotional control,

irritability, and perhaps sweating or colour changes. They may never make a reasonable adjustment to flying, and are more than usually liable to gastro-intestinal disturbance. They may rapidly become devastatingly *airsick* and lie prostrate for hours after they have struggled or been helped to recumbency at the airport after arrival. To some extent these phenomena represent an idiosyncrasy. A clue to their possible appearance can sometimes be obtained from conversation with an individual or from consideration of his previous history, with emphasis on car and train sickness, fainting, and other manifestations of vasomotor instability or exaggerated response to emotion. How far-reaching the effects of air sickness may be in an individual already partially disabled can be imagined, and the particular importance of gastro-intestinal ulcerative conditions in this respect needs no stressing.

Fatigue.—All travel is exhausting, air travel particularly so. This is due not only to its strangeness or to subdued nervous tension. Even for the seasoned air traveller a journey of two or three hours spent in the perusal of illustrated papers or the lightest of literature, refreshed perhaps by sandwiches and a whisky, can be very tiring. Further, it may be necessary for safety considerations to abandon the schedule, vary the route, and spend some hours in out-of-the-way places where it would be uneconomical to provide elaborate hotel facilities. In fact, it will readily be understood that in some instances the facilities, if adequate, are yet crude. In certain parts of the world and at certain seasons the most favourable conditions for flying occur in the early part of the day, and it may be that a dawn take-off will be scheduled two or three days running. There may be some distance to be traversed between the hotel or rest house and the airfield, so that the night's rest is short and apt to be broken. Again, if dogged by really bad luck, some technical fault not discovered until the final proving just before take-off may cause postponement, even after the passengers have arrived at the airfield. This sort of hazard in air travel increases nervous tension, and although it may have no more than a nuisance value to the ordinary experienced passenger, it is sometimes a dominating factor when considering air travel for individuals with a physical disability.

MEDICAL CONSIDERATIONS

When considering in detail medical contraindications to flying, it is useful to think of the potential travellers as being divided into two groups. In the first group are those people, up and about and often working, yet possessed of some disability. Of this they may be unaware, or they may know of its existence and therefore seek advice about their fitness for flying, although they may not necessarily consult a medical man connected with the air line. Again, they may know of it and deliberately conceal it. In doing so they may be taking upon themselves a very grave responsibility. If during flight a passenger becomes urgently ill for any reason, a decision may be forced upon the captain of the aircraft as between the life of a patient *in*

extremis and the safety of the aircraft and all its occupants, which might be jeopardized by an *ad hoc* alteration in the flight plan. It is quite wrong and unfair to the pilot that he should be confronted with such a situation developing, as it does, out of deliberate concealment of a disability. In this group, the existence of a disability is not known to the airline, and it is in order to assess the risks involved that some of the insurance companies require a medical examination before accepting passengers for cover.

The second group is made up of individuals who are definitely patients, more or less invalids, for whom a journey becomes necessary so that they may obtain a change of climate or some special form of treatment. It will be quite obvious that a patient is to be a passenger, and special arrangements will have to be made for transport to and from the aircraft, and for accommodation on the route. The airline therefore has the opportunity to say whether or not they will accept the liability.

FIRST GROUP—'CRYPTOPATHS'

Of the first group, it may be said at the start, that there are very few (other than those who show cardiac and respiratory disorders, to be mentioned later) who are not able to travel by air. If their health is such that they could undertake a journey by rail or road of two or three hours' duration, then there is probably no reason why they should not travel for an equivalent length of time by air. Longer journeys, with the factors of exhaustion, uncertainty of schedule, and the possibility of bad weather, require more careful thought. A high priority would be given to these considerations (which are rather those of air travel than of flying as such) in the case, for instance, of a young, fairly severe diabetic stabilized on diet and insulin, in whom control can be lost, even without air sickness, by inability to carry on with meals and injections according to his normal routine. The difficulties need not be insurmountable, but it would be necessary to select such a patient very carefully and to be sure that he was a person with sufficient knowledge and experience of his condition to be able to keep control of it by his own initiative.

When considering *cardiac conditions* in ambulant individuals (and, indeed, this is true of all disabilities) it must be borne in mind that if any harm does befall these people while they are flying, the mishap will surely be laid at the door of air travel. Heart disease, with good tolerance of everyday activity, is no contraindication, and children with congenital valvular defects with cyanosis have made successful journeys by air. Hypertension *per se* need not be any contraindication, although if the figures are very high (systolic in excess of 220 mm.), then air travel does carry some risk for them, especially if they are emotionally labile and it is their first trip. Headache at altitude is a feature of hypertension. If there are symptoms clearly attributable to hypertension, or if there is evidence of associated

effects of cardiac ischæmia, then such persons should be advised against travelling by air. This rules out individuals liable to attacks of angina pectoris, and patients should not travel by air within four months of being diagnosed as having suffered a cardiac infarct. Disturbances of rhythm of themselves need be no bar, particularly if they are well under control. A tendency to paroxysms of tachycardia, if these have been experienced quite recently, may raise doubts even in an otherwise normal individual.

Chronic and recurrent *respiratory conditions* in ambulant patients present another problem. In the case of patients giving a history of spasmodic asthma, despite assertions that individual asthmatic attacks benefit by altitude, the answer is by no means simple. If the patient is passing through a phase of frequent attacks and is of unstable temperament, then air travel is certainly contraindicated, but in the absence of some such definite complications they would probably be considered as fit. Established emphysema must always raise doubts, and if middle-aged or elderly people are breathless on slight exertion from this cause they should be advised against travelling by air. Acute conditions of the upper respiratory tract, coryza or catarrh, may give rise to complications because of altitude. Considerable pain may be experienced in connexion with one or other of the paranasal sinuses, and the inflammatory changes which may result can give rise in the case of the sinuses or the middle ear to the usual far-reaching consequences.

Any lesion in the chest which occupies space may be a contraindication, and although cases of pleural effusion, empyema, intrathoracic neoplasm, and hæmothorax have all been carried by air and will doubtless be carried again, this should not be recommended without careful thought and weighing up the pros and cons. An individual with one pleural space half filled with fluid is in danger on this account alone, and a prolonged severe spasm of coughing can quickly change his state from one of relative calm and comfort to one that is critical and urgent and may sometimes prove fatal. Because of the risk of rupturing into the lung, the empyema is the least desirable of these conditions to permit travel by air. Cases of pulmonary abscess and infected bronchiectasis with much sputum are unsuitable, and large lung cysts or bullæ also constitute a contraindication. There is, perhaps, no theoretical reason why they should be, but experience has shown, as with the empyema, that their journeyings are not free from complications.

Pulmonary tuberculosis presents its own special problems. From the point of view of the public health any airline company might refuse to carry a patient suffering from a potentially infective condition. This will automatically rule out most cases of active pulmonary tuberculosis, and, indeed, in their own interests such patients should not travel by air. The pressure changes which they may encounter lay them open to the risk of at least spread, and perhaps hæmorrhage, particularly in connexion with tension cavities. Air travel for people with a *pneumothorax* or *pneumoperitoneum*

(and this applies also to ambulant individuals who are in full employment) is a risk which no physician should accept unless very special arrangements can be made. The fact that in some instances people with a pneumothorax have made a journey by air "successfully" is no argument for permitting it, for the harmful effects of altitude upon pneumothorax have been demonstrated beyond a peradventure (Todd, 1943). Although this is a good general rule and patients with a pneumothorax should be vigorously discouraged from taking journeys by air, there may be occasions when it is necessary, in which event they should travel before a refill is due rather than immediately after one. Altitude above 5000 ft. may have dire consequences for them but, if air travel is absolutely essential, its effect can be offset if there is a medical man ready at hand with apparatus to aspirate air from the pneumothorax. A history of recurrent spontaneous pneumothorax is a contraindication, and patients with traumatic pneumothorax will always require careful and expert handling if they are to travel by air.

The fact that patients with *anæmia* travel badly has received wide recognition, and severe degrees of *anæmia* certainly constitute a contraindication to flying. Fatalities occurred even in evacuation by hospital train of patients with *anæmia* during the war, and a good working rule was that cases should not be moved if the hæmoglobin was less than 7 gm. per 100 c.cm. (roughly 50 per cent. Haldane). There is some evidence, too, that the conditions encountered in air travel may precipitate an attack of *renal colic* in a patient with renal stones. The wisdom of such patients travelling by air may well be open to doubt if a long journey is contemplated.

SECOND GROUP—"PATIENTS"

Generally speaking, the need to move by air acutely ill or injured people will not arise under peace-time conditions. There may, however, be circumstances which demand its consideration. In this connexion there is a mass of material in the shape of the records of air evacuation of casualties (Stewart, 1945; Jackson, 1945). The majority of these were traumatic, the injuries having been sustained by fit and in the main young men, whose case is rather different from that of an illness which arises from within. In the early days of a campaign the same standard of care could not be applied in forward areas as obtained at base, and base or even home could be reached provided the "risks" of air travel were accepted. The patients themselves were generally thankful that the chance of a "flip home" had come their way, an attitude in itself tending to minimize the complications of air travel. In B.L.A. one R.A.F. group alone evacuated 116,700 casualties between D and VE day without a single loss. Air sickness occurred in 1.2 per cent., and of these the majority were the walking wounded who sat in the rear of the aircraft. Among 979 casualties arriving at a certain field, 15 only were found to be unfit for further travel and in need of admission to the casualty air evacuation centre forthwith for resuscitation and treatment. These in-

cluded a varied selection of cases, all of them post-traumatic, save one who was suffering from severe malaria.

This experience really epitomizes the position in regard to medical contraindications to flying. Each individual case presents its own problem, and each must be judged on its merits. Although more generally applicable under war-time conditions than in peace, expediency is a most potent consideration. After weighing up all the pros and cons it may be clear that, despite the drawbacks of air travel for a given individual or patient, the anticipated gain is well worth all the hazards and chances. Under war-time conditions in South East Asia, the gain to be derived, for instance, from evacuating a case of pulmonary tuberculosis from Ramree Island before the monsoon might far outweigh the risks of air travel in this disease, and even justify the exercise of discretion in the matter of the contravention of a Command directive. Even in peace time in civilian life, it may well be found, in a given case, that the advantages to be gained by transporting a patient to the right place quickly are paramount and override all objections.

SUMMARY

If any member of the public is in doubt about his fitness for air travel he would be well advised to ask his doctor. It is very wrong of anybody to conceal a disability, since to do so may have the gravest consequences for the rest of the passengers, the aircraft and crew. The medical man whose advice is sought about an individual's fitness for travel must first consider those features peculiar to air travel, and secondly, should try to assess those factors in his patient's make-up which may operate to his disadvantage in aviation. Despite all drawbacks air travel may, in certain instances, constitute a justifiable risk, and on the whole invalids travel well. Among the conditions which ordinarily constitute contraindications to flying on medical grounds may be mentioned hypertension, angina pectoris, recent myocardial infarction, recurrent asthma, emphysema, acute upper respiratory catarrh, most space-occupying intrathoracic lesions, and pulmonary tuberculosis, especially if the patient is undergoing treatment by pneumothorax or pneumoperitoneum.

My thanks are due to the D.G.M.S., R.A.F., to the P.M.O. Transport Command, R.A.F., to Air Vice Marshal Rook, and to the D.M.S., B.O.A.C., for their help and for allowing me access to records and other material in their Departments.

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asthma has not been much stressed, and yet, if the analogy is a good one, this might not be an unprofitable line of approach. Have we any counterparts to phenobarbitone, epanutin, and tridione with which we could continuously damp down the over-excitability of bronchial musculature or the nervous influences which play upon it? Before considering this, let me summarize briefly the other accepted lines of preventive treatment in asthma.

PREVENTIVE MEASURES

First, there is the method of *desensitization*, both specific and non-specific, based on the theory that asthma is allergic in origin. The results are not statistically satisfactory; the patient usually relapses as before. It seems that the devil which is asthma can outwit the most enthusiastic allergist, and the patient is always in the process of becoming sensitive to something new. Moreover, it was shown before the recent war, at Guy's Hospital, that equally good results could be obtained with distilled water injections as with desensitizing solutions, in both series the patient receiving the same general treatment. This observation, which was very carefully controlled, has been said to be the only real advance in knowledge of the treatment of asthma in the last fifteen years!

Secondly, there is the *psychological approach*, which has rightly received a great deal of attention. Asthmatics often volunteer that they are nervous and excitable and that emotion may bring on their attacks. Children with asthma are frequently described as being retiring, dependent, and over-protected by their mothers. My view is that although asthmatics are as a rule highly strung, most of the traits ascribed to them are secondary to their complaint. Anything more calculated to cause panic or a sense of inferiority in a child than inability to draw breath can hardly be imagined. I am unable to subscribe to the view that asthma is primarily psychological, and such statements as "asthma is at one and the same time a desire for and a revulsion from the sexual act" leave me cold. However, the commonsense attitude is very important. In those cases in which the trigger is a psychological one, anything that stabilizes a patient's domestic affairs may help to minimize attacks; further, a child and his parents can be greatly helped by the strong reassurance that the attacks are harmless, despite their terrifying nature. Finally, much can be done by encouraging asthmatics to lead as normal a life as possible: measures such as playrooms, for example, where children can be encouraged to mix and enjoy themselves, can do nothing but good.

TREATMENT

Specific treatment is the most important part of the management of asthma. By means of the pharmacopœial preparations which are available it is *usually* possible to control the disease, and with adrenaline, aminophylline, and ephedrine there is almost as good an armamentarium for asthma as there is for epilepsy. It must be remembered, however, that these drugs only pre-

ASTHMA: A NOTE ON PREVENTIVE TREATMENT

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A SLIGHT consolation for being roused from bed to treat a patient with asthma is that it is at least possible to do something. A few minims of the magical adrenaline, the spasm usually passes, and both patient and relatives are able to draw breath again. But the problem of asthma remains, for it is the problem of the relapse. How can asthmatics be kept well? Volumes have been written on the subject, but there has been as yet no satisfactory answer, and the innumerable treatments recommended all tend to be vitiated by the natural proneness of the disease to remission. Is the patient better *propter* or only *post hoc*? Now it has always seemed to me a very curious fact that a disease which has such a specific treatment (adrenaline) once it has developed, should baffle all attempts to prevent it. When faced with a difficulty such as this, it is useful to see if help can be obtained from analogy. Consider, for example, other specifics—insulin for diabetes, liver for pernicious anæmia, digitalis for auricular fibrillation, and phenobarbitone for epilepsy. The following facts stand out about them all:—First, continuity of treatment is essential; secondly, after an initial period of intensive therapy a maintenance dose is arrived at, and this does not usually need to be increased; thirdly, the patient is able to lead a more or less normal life, and the taking of his specific becomes no more an addiction than does cleaning his teeth or drinking his tea. Applied to asthma, this would mean that any specific would probably need to be taken in maintenance doses for indefinite periods, but patients could be reassured that they were not becoming drug addicts.

Let us now see whether any of the diseases with specific remedies resembles asthma in any way. Surely epilepsy is a first cousin. In both there is paroxysmal dysrhythmia—periodic violent outbursts occurring suddenly and often with no obvious explanation, and alternating with cycles when the patient is usually in normal health. Both have a familial tendency, and both often start following infectious diseases. Both may be aggravated or modified by menstruation or pregnancy. In both, psychological factors may provoke attacks. Both may be grown out of at puberty. Both may have an aura, and in both continuous attacks give rise to status epilepticus and status asthmaticus, respectively. Finally, in both there is a small residue of unfortunates in whom treatment is of no avail. The similarity between the two diseases has often been noticed before but generally with a view to explaining epilepsy on an allergic basis, usually without success. By comparison, the application of the principles of the treatment of epilepsy to

that it should not be discontinued even after the attacks have stopped. I advocate, as in epilepsy, that the drug should be continued until a patient has been clear for two years. It rarely has any side-effects, and the remarkable improvement in the patient's general condition when the regular nocturnal attack is prevented is most gratifying. Weight goes up, appetite improves, and the patient increasingly begins to be able to do more. Three minor points I have noted with this particular compound:—First, the patient may sometimes still wake up at 3.30 a.m., sneezing instead of having asthma. This phase passes after a few weeks. Secondly, the drug sometimes “pushes the asthma on”, so that attacks occur during the morning instead of in the night. In this event a second dose, given on waking, is generally successful. Thirdly, occasionally the ephedrine in the preparation causes the patient to be wakeful. This can be counteracted by increasing the relative proportion of phenobarbitone in the tablet. Sometimes patients are better suited by aminophylline alone, and theamin (Eli Lilly) is a useful alternative, but it must be given in the same way, continuously. Hurst thought that the introduction of aminophylline in the treatment of asthma was the greatest advance since adrenaline. I think this still holds—the newer antihistamine drugs, benadryl, antistin, and anthisan being most disappointing in asthma.

ILLUSTRATIVE CASES

With the object of investigating the continuous treatment hypothesis I have followed up forty-five patients who have been on continuous suppressive treatment and inhalation for not less than four months. Patients who had other forms of treatment as well are excluded. The cases were assessed and grouped after two months' treatment, and again at not less than four months, the longest period of observation in any one case being eight months. Anyone who has tried to follow up cases of asthma knows how difficult it is to assess fluctuations in the patients' health unless there is a dramatic change. Patients may say they are improved but reference to their records shows that they are having just as many attacks as before; conversely, a patient may say he is “never free”, and yet his family's report belies him. The Asthma Research Council has tried to get over part of this difficulty by dividing asthmatics into five grades of severity, and improvement is not recorded unless the patient has moved up at least one grade.

In Grade 1 the asthma is continuous and of such severity that the patient is unable to do ordinary duties or to attend school.

In Grade 2 the asthma is continuous but, although wheezy, the patient is able to do ordinary duties or attend school at least three-quarters of the time.

In Grade 3 asthma is not continuous but attacks occur at least once a month or, alternatively, are markedly seasonal. (Groups 2 and 3 form the bulk of any clinic.)

Grade 4 contains those in whom asthma is not continuous and in whom attacks occur less frequently than once a month.

Grade 5 is reserved for those who have had no attacks for a year at least, active treatment having ceased for six months.

Moving up one grade is recorded as slight, two as moderate, and three as marked, improvement.

vent or relieve asthma. They are of little use for the cough and shortness of breath which are the result of the associated bronchitis and emphysema. Most asthmatics have discovered the usefulness of drugs for themselves, and it is a point to be remembered, when assessing the results of any other form of treatment, that there is a chemist's shop by the bedside of every wheezer in the country! What is the proper use of these valuable weapons?

(1) Every asthmatic should try the effect of an inhaler. There are various types on the market; I prefer one with a face-piece. The ingredients of the inhalant vary, but on the whole the proprietary blunderbuss preparations, containing adrenaline, pituitrin, atropine, and papaverine are better than the simple 1:100 adrenaline. The usefulness of the inhaler is that it relieves minor wheeziness, and the knowledge that the patient has a specific to deal with any slight disability is most helpful. The inhaler is, strictly speaking, a preventive only in the sense that it usually prevents minor attacks from becoming major. Objections have been raised to it on the grounds that (a) *the more it is used the more it is needed. This is not my experience.* (b) *That its continued use may damage the bronchial mucosa. This may be so, but in my view it is an academic theory as opposed to the certainty of incurable emphysema which results from long-standing untreated asthma.*

(2) Every asthmatic should be taught how to give himself adrenaline subcutaneously. This will abort many severe attacks. For some extraordinary reason patients and often doctors are loth to use this form of treatment, mainly because it is thought to be habit-forming and that larger and larger doses will become necessary, and also because of its side-effects, which are the result of giving the drug too quickly. My answer is:—Who would ever think of denying a severe diabetic insulin? The most common fault with regard to adrenaline is that enough is not given, and in hospital it is fatal to write up "adrenaline, minims 10 s.o.s.", because the patients never get it until they are practically suffocating. Sisters and nursing staff reflect the prevalent view that asthma is synonymous with "nerves" and that every effort should be made to do without the drug. Exactly the reverse is the case. So far as I know, there are no dangers in the treatment, but occasionally the patient, after many weary days of status asthmaticus, may become temporarily adrenaline-resistant.

(3) Even when the patient is well he requires treatment, and he should be given a maintenance dose of a suppressive drug indefinitely, just as in epilepsy. We have tried out a considerable number of preparations, and the one which gives the best results is a compound of aminophylline, ephedrine, and luminal, marketed under the trade name of "franol" (Bayer). The three ingredients act respectively on the bronchial musculature, the nerve endings, and the central nervous system, and there is probably some potentiation since the dose of each individual component is small. Its most striking effect is in suppressing those nocturnal attacks which may occur night after night with clockwork regularity. It is less effective in preventing chronic wheeziness. The dose is usually one tablet at night, and the great point is

I have tried to adopt this principle in assessing my series, although it was difficult in some cases to be sure of the categories. The group as a whole may be regarded as being a compound of moderately bad asthmatics, since 39 belonged to groups 2 or 3 (16 to group 2; 23 to group 3).

Briefly, I found that at two months three-quarters of the patients had improved, using the Asthma Research Council's definition, about a third becoming entirely clear. At the end of at least four months the improved patients were re-assessed and were found to be either in the same improved category or to have still further improved. No one who had improved after two months relapsed sufficiently to be down-graded at four months. In other words, if the patients were going to improve at all they improved very quickly, and if the treatment was kept up they remained better. We found, like other investigators, that the patients who did best were those who were young, those in whom the attacks occurred infrequently or at one particular time of day only, and those in whom the disease was not of long standing. The non-improved group is made up of older asthmatics with a long history, patients with emphysema, and a residue of those in all age-groups in whom the treatment just did not work.

The only point that needs stressing in my group of cases is that the *relapse* rate is considerably less than in other series of patients who had similar general treatment, but who had only had it intermittently for attacks. In these circumstances the relapse rate after six months was of the order of 25 per cent. This approach to asthma is somewhat defeatist in that it may tend to distract attention from the finding of the essential causes of asthma. This, of course, must be done, but it is possible by the above method of treatment to improve most asthmatics and to keep them in reasonable health. If while they are improved, further search reveals specific causes which can be dealt with, so much the better.

Having analysed these cases, my views about the similarity between asthma and epilepsy have been still further strengthened. Gowers (1901) wrote of epilepsy that the outlook was best when the fits took place at a regular time in the twenty-four hours, particularly at night, when the patient was young, and when the disease was not of long standing. Arrest is also much more likely when the continuance of education and of regular employment allows of a fully occupied and satisfying life. It is much less when education is discontinued, pleasures and sports are forbidden, and the patient is condemned to a narrow life of frustration. Could anything be a more accurate description of the factors influencing prognosis in asthma?

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I have tried to adopt this principle in assessing my series, although was difficult in some cases to be sure of the categories. The group as a whole may be regarded as being a compound of moderately bad asthma since 39 belonged to groups 2 or 3 (16 to group 2; 23 to group 3).

Briefly, I found that at two months three-quarters of the patients had improved using the Asthma Research Council's definition, about a third becoming entirely clear. At the end of at least four months the improved patients were reassessed and were found to be either in the same improved category or to have still further improved. No one who had improved after two months relapsed sufficiently to be down-graded at four months. In other words, if the patients were going to improve at all they improved very quickly, and if the treatment was kept up they remained better. We found, like other investigators, that the patients who did best were those who were young, those in whom the attacks occurred infrequently or at one particular time of day only, and those in whom the disease was not of long standing. The improved group is made up of older asthmatics with a long history, patients with emphysema, and a residue of those in all age-groups in whom the treatment just did not work.

The only point that needs stressing in my group of cases is that the relapse rate is considerably less than in other series of patients who have had similar general treatment, but who had only had it intermittently during their attacks. In these circumstances the relapse rate after six months was of the order of 25 per cent. This approach to asthma is somewhat defeatist in that it may tend to distract attention from the finding of the essential causes of asthma. This, of course, must be done, but it is possible by the application of the method of treatment to improve most asthmatics and to keep them in reasonable health. If while they are improved, further search reveals specific causes which can be dealt with, so much the better.

Having analysed these cases, my views about the similarity between asthma and epilepsy have been still further strengthened. Gowers (1901) wrote of epilepsy that the outlook was best when the fits took place at a regular time in the twenty-four hours, particularly at night, when the patient was young, and when the disease was not of long standing. Arrest is much more likely when the continuance of education and of regular employment allows of a fully occupied and satisfying life. It is much less when education is discontinued, pleasures and sports are forbidden, and the patient is condemned to a narrow life of frustration. Could anything be a more accurate description of the factors influencing prognosis in asthma?

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The symptoms diminished in a week, and in a second series of patch tests with perchloride of mercury the response was "questionable or negative". Sulzberger and his colleagues claim that this is the first reported case of eczematous allergy in which successive patch tests revealed a loss or diminution of allergic skin sensitivity occurring rapidly, despite or because of continued exposure to the allergen, and coinciding with a remission of clinical allergic reaction in a site still exposed to the causative agent. It is noteworthy that this case also did not react to patch tests with cinnabar. Swinny (1946) recorded the details of a case in which a man was tattooed at the age of sixteen. Fifteen years later, after a period of three years during which he suffered from urticaria, he developed a widespread weeping and exfoliative dermatitis. The red areas of his tattoo were itchy and became swollen if gently rubbed. Patch tests showed that he was sensitive to 2 per cent. ammoniated mercury ointment and to 1:1000 perchloride of mercury. His eruption disappeared two months after the tattooed areas were excised.

It is known that the pigments inserted in tattooing tend to accumulate in the deeper layers of the dermis near the blood vessels; much of the pigment is free but some is intracellular (Desaux, 1948). If the particles are insoluble they persist indefinitely. It is possible that the intra-cellular particles may undergo some dissociation and form organic chemical compounds with certain substances in the cells, in which event they may perhaps act as haptens. The fact that in two of the recorded cases negative patch tests to cinnabar were obtained would seem to indicate that dissociation of the compound is necessary if a reaction is to occur. As the dissociation probably affects only minute quantities of the cinnabar, this presumably explains why the symptoms disappear quickly, for the metabolic activity of the skin probably causes the rapid disappearance of the compounds.

The cause of the sudden flare in the queried case is unknown, but it would be interesting to ascertain if the symptoms could be reproduced by bathing a small area of his red tattoo with a petrol similar to that to which he was exposed. If the symptoms of inflammation recurred this might be due to the presence of mercury or sulphur in the petrol (unlikely) or to the absorption of some fraction of petrol by the skin which causes liberation of mercury or sulphur from the cinnabar in the corium. It is possible that the reaction was due to the use of a mercurial lotion or ointment (as in Unna's case) or to taking a mercurial purgative, such as calomel or grey powder.

This inquiry and the difficulty which I have had in obtaining information about tattooing prompt me to add that a monograph giving ethnological, psychological and chemical information as well as practical details on how to become an expert tattooist would fill a gap in our knowledge and provide a readable book likely to be of considerable interest. A classical work was published in Paris in 1881 by Lacasagne, entitled "Les Tatouages", and General Robley in 1896 published a book on "Moko or Maori Tattooing", but in recent years the subject does not appear to have received much attention.

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THE SEVENTH BRITISH PHARMACOPŒIA

By WILLIAM A. R. THOMSON, M.D.

IN these days of change and austerity it is a joy to handle the new *British Pharmacopœia*, with its familiar red cover bearing the Royal Coat of Arms. The seventh *British Pharmacopœia*, which comes into force as from September 1, 1948, is of particular interest, as its publication has been delayed on account of the 1939-45 war. The one which it is about to replace was published in 1932, and it was intended that successive issues should be published at intervals of ten years, suitable provision being made during the decennial intervals for supplementing the current issue by the publication of Addenda. Although in September 1939 the new Pharmacopœia was well under way, it was decided that it would be impracticable to proceed with its completion under war conditions. As a substitute, frequent Addenda were published for the two-fold reason of keeping the Pharmacopœia reasonably up to date and to provide substitutes for, or alternatives to, substances which were unobtainable because of the war. The first Addendum had already been published in 1936, and subsequent ones were issued in 1940, 1941 (two), 1942, 1943 and 1945. This multiplication of Addenda, although undoubtedly necessary and, under the conditions, desirable, has not eased the life of pharmacists, and their replacement by the new Pharmacopœia will be welcomed by all who are actively concerned with the preparation and dispensing of drugs.

The main interest of the new Pharmacopœia, however, is the striking commentary it provides on the advances in therapeutics that has taken place since 1932. Ever since the first *British Pharmacopœia* was published in 1864, each new one has had to undergo radical alteration and revision, but there can be little doubt that, in the words of the preface to the latest one, its preparation "has, it may be said with confidence, been a more complex and laborious task than the preparation of its predecessors". The pages now number just under 1000, an increase of practically 200 compared with the 1932 issue. There are now 774 monographs, an increase of 187, and of these 155 are entirely new. As evidence of the radical revision that has been carried out, it may be mentioned that 145 monographs of the 1932 issue and its Addenda have been discarded.

SOME CHANGES

Of the many additions to the new Pharmacopœia, the most striking is the large number of injections now included—fifty-seven, compared with six in the current issue, and of tablets—eighteen, compared with only one in the 1932 issue. Among the new additions mention may be made of the œstrogens, methyl testosterone and testosterone propionate, protamine zinc insulin, thiouracil and methylthiouracil, pethidine, picROTOXIN, dicoumarol, tryparsamide and aminophylline, as well as various penicillin preparations. Some

curious deletions include sulphapyridine, hexamine and Easton's syrup.

There are also certain changes in nomenclature which should be noted. For instance, "*Aqua sterilisata*" is now known by the more cumbersome, if more accurate, name of "*Aqua pro injectione*"; powdered digitalis as prepared digitalis, and strophanthin-G is now christened ouabain. Certain preparations hitherto named "soluble —" are now to be known as the sodium salt; e.g. soluble sulphathiazole is now named sulphathiazole sodium; this also applies to hexobarbitone, pentobarbitone, phenobarbitone, and thiopentone.

There are now six sulphonamides in the Pharmacopœia, i.e. succinylsulphathiazole, sulphacetamide (and its sodium salt), sulphadiazine (and its sodium salt), sulphaguanidine, sulphanilamide and sulphathiazole (and its sodium salt). Penicillin is included in the form of the calcium and sodium salts, the cream and sterilized cream, the injection, the oily injection, lozenges and the ointment.

When the function of the Pharmacopœia is considered, it is clear that considerable care must be exercised before well-tried remedies are discarded. Similarly, a moment's thought will show that in view of the vast number of investigations and experiments that have to be carried out in preparing a new issue, there must be a considerable time-lag between the introduction of new remedies and their final installation in the Pharmacopœia.

THE METRIC AND IMPERIAL SYSTEMS

There is still no evidence of the British Pharmacopœia Commission being prepared to take a strong line in the question of the general adoption of the metric system. Doses are expressed both in the metric system and the Imperial system. Whilst there is clearly much to be said in favour of an official publication such as this adopting a cautious attitude in this matter, it is perhaps to be regretted that advantage was not taken of the opportunity offered by the introduction of some of the newer synthetic preparations to give their dosage only in the metric system. Preparations such as dicoumarol, deoxycortone acetate, mersalyl and stilbœstrol, for instance, are almost universally prescribed according to the metric system. To give their dosage in the Imperial system as well, is not merely pedantic, it can well be regarded as a retrograde step.

In the metric system, weights are given in multiples or fractions of a gramme or of a milligram, whilst fluid measures are given in multiples or fractions of a millilitre. In the case of weights a sound working scheme has been adopted: quantities of 0.1 gramme or more are expressed as grammes or fractions of a gramme, smaller quantities being expressed as milligrams or fractions of a milligram. The abbreviations used are: "G." for gramme, "mg." for milligram, and "ml." for millilitre. On the recurring controversy of the relative value of the cubic centimetre and the millilitre, a common-sense compromise is adopted: "The unit of volume denoted by the term 'cubic centimetre' . . . differs from a millilitre by so small an amount that the difference may be disregarded for all ordinary purposes".

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It is to be hoped that practitioners will adopt the advice given on the use of symbols in prescriptions: "In prescriptions the symbol \mathfrak{z} i has been used to represent 60 grains, and also to represent 1 fluid drachm; and the symbol \mathfrak{z} ii to represent sometimes 480 grains and also to represent 1 fluid ounce. As these symbols are apt to cause confusion, it is recommended that their use be discontinued. Instead, when the Imperial system is employed in prescribing, solids should be prescribed in grains (gr.) and ounces (oz.=437.5 grains), and liquids in minims (m.) and fluid ounces (fl. oz.); and the quantities should be written in Arabic numerals. In order to avoid the possibility of confusion between gramme and grain the symbol G. should be used in prescriptions as the contraction for gramme".

SOME PRACTICAL POINTS

So many complaints are heard these days concerning the standard of prescribing, that perhaps attention should be drawn to some important practical points in the Pharmacopœia. The official names of all drugs, preparations and other substances are given in Latin and in English. It is sometimes forgotten that the English title is as much an official title as the Latin one. The English title is the English name in common use and is not necessarily a literal translation of the Latin title. Official abbreviations of the Latin titles are provided. In using abbreviations it is clearly advisable that only the official ones should be used. The position is well summarized in the "General Notices" which introduce the Pharmacopœia: "For the convenience of the prescriber and the dispenser, it is desirable that, if an abbreviation of any Latin title is used, it should be the abbreviation of the British Pharmacopœia". Alternatively, might one make a plea for the more general use of the English titles?

Attention is again drawn to the inadvisability of prescribing medicines in terms of domestic measures, such as teaspoons, and so forth. It is desirable that graduated glass measures should be used, graduated in millilitres or minims and fluid ounces, and that doses be prescribed in these units, instead of the traditional teaspoonsful and so forth. Finally, it may not be out of place to remind practitioners that "when an unusually large dose appears to have been prescribed, it shall be the duty of the pharmacist or dispenser to satisfy himself that the prescriber's intention has been correctly interpreted".

Taken all in all, this is a work of which the British Pharmacopœia Commission has every reason to be proud. It not merely maintains, but indeed enhances, the reputation of its predecessors. Both in discarding the old and in absorbing the new, outstanding judgment and discrimination have been shown. The standard of production is equally high. Unfortunately the Treasury, responsible for fixing a price, has not been able to emulate the efficiency of the Commission, with the result that it is not yet possible to state the price at which the volume will be available.

CURRENT THERAPEUTICS

VI.—CHEMOTHERAPY OF CANCER

By JOSEPH S. MITCHELL, M.B., PH.D., D.M.R.

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THE limitations of radiotherapy and surgery are such that the need for effective chemotherapy of malignant diseases is one of the urgent requirements of medicine. The problem is much more difficult than that of bacterial infections, probably because of the remarkably close biological similarity between the malignant and normal cells and the related absence of protective mechanisms against the abnormal cells. It seems unlikely that any generally useful solution, if such exists, will be reached for many years. The history of the subject suggests that significant advances are most likely to come from developments from fundamental research in subjects not obviously related to the chemotherapy of cancer.

At the present time, there is probably no method of *radical*, meaning permanently curative, chemotherapy for any type of cancer or allied disease. Perhaps the synthetic oestrogens will permanently control some cases of carcinoma of the prostate, but this has yet to be proved. It seems impossible to repeat the interesting results claimed to have been observed at the end of the last century in intercurrent infections or with Coley's mixed bacterial toxins. So far, excluding surgery, radiation is the only agent which has produced permanent healing in any substantial number of cases of malignant disease and, although further improvements are likely, the limitations of radiotherapy are now well recognized. Understanding of the mechanism of the therapeutic action of radiations has been an important influence in recent work on chemotherapy. Probably the most important mechanism by which radiations kill cells is the production of gross structural changes in the chromosomes, following chromosome breakage, reunion and interchange. Mitotic inhibition *per se* appears to be less important. On the biochemical side it has been shown that therapeutic doses of radiations inhibit the synthesis of thymonucleic acid and everything points to a far-reaching metabolic disturbance, the investigation of which is in its infancy, but which nevertheless is likely to be very important for the development of chemotherapy. It seems that one useful line of approach may be the combination of radiation and chemotherapeutic agents.

Within the last ten years, a definite approach has been made to practical, although limited, *palliative* chemotherapy, which as yet has been found useful mainly in some of the less common diseases. Some of these agents may not stand the test of time but, within their limitations, mark real advances. Points of importance brought out by recent work are the specificity of different therapeutic agents in different diseases and the difference in response to different agents shown by individual cases of apparently the

same disease. The clinical evaluation of any agent of real chemotherapeutic promise in this field, especially if used in combination with radiotherapy, involves painstaking clinical and laboratory investigation of adequate numbers of patients for at least three to five years, with systematic follow-up, which can be continued indefinitely if necessary, and if possible with adequate controls. Only critical clinical investigation of this type, with the best possible treatment of the individual patient, will provide correct assessment of the therapeutic value of any agent which appears to continue to be useful. While not minimizing the value of genuine temporary benefit from any particular treatment, one must avoid the pitfalls of uncritical acceptance of new remedies. The history of the chemotherapy of cancer provides a very sad warning. Nevertheless, there are a few practical chemotherapeutic agents which can be justifiably used in some cases. These may be classified as follows:—

- (a) Radio-active isotopes, especially radiophosphorus and radio-iodine.
- (b) Radiomimetic chemotherapeutic agents, viz., the nitrogen mustards and urethane.
- (c) Hormones and hormone-like agents, especially stilbæstrol and testosterone.
- (d) Miscellaneous agents, of which arsenite, and stilbamidine and pentamidine are the most important.

There are, of course, many other substances of contemporary interest, including bacterial polysaccharides, colchicine derivatives, α - β -diphenyl ethylamines, acriflavine, auramine, 2-methyl-1-4-naphthahydroquinone diphosphate, toluidine blue and teropterin, for which as yet no assessment of the therapeutic value when used alone or in combination with radiations is available. The literature is voluminous, but two recent general surveys may be mentioned (1, 2).

RADIO-ACTIVE ISOTOPES

It can now be accepted, mainly as a result of American work, that radiophosphorus, P^{32} , used as inorganic phosphate (3-11), and to a much smaller extent—at least so far as malignant condition are concerned—the radio-iodines, especially I^{131} (9, 12-17), can be justifiably employed as therapeutic agents for internal medication in suitable cases.

The chemotherapeutic use of radio-active isotopes is essentially a form of radiotherapy and, in general, will require the experience of a radiotherapist and the collaboration of a physicist trained both in radiotherapeutic dosimetry and the techniques of handling and measurement of radio-active isotopes. The clinical problems include those met with in the use of external radiation, and further, it is essential to correlate the dosage of the radio-active isotope with the radiation dose in roentgen units (18,19) received by both the abnormal cells and the normal radiosensitive cells, especially those of the bone marrow and reproductive organs. The risks of administering internally any radio-active substance must be studied and estimated in each case, and the protection of both personnel and patients must be carefully planned and supervised.

Radiophosphorus.—Radiophosphorus, P^{32} , has a half-life of 14.3 days and emits only *beta* particles, the average energy of which is 0.70 million electron volts. It is usually administered intravenously in the form of an isotonic solution of Na_2HPO_4 containing initially at least 300 microcuries of P^{32} in 15-18 mgm. of anhydrous Na_2HPO_4 per c.cm. If supplied in the form of potassium salts, it has usually been given by mouth. Oral administration is apparently satisfactory if the phosphate solution is administered two hours before breakfast with avoidance during the period of treatment of iron compounds, alumina and milk. Under these conditions, it is usually assumed that 75 per cent. of the radiophosphorus is absorbed.

With regard to dosimetry, it can be shown that for P^{32} , (a) 1 microcurie per gm. of tissue delivers a dose of 38.5r per 24 hours at constant concentration; (b) neglecting excretion, 1 microcurie destroyed per gm. delivers 795r and 1r is delivered by 1.26 microcuries destroyed per kilogram of tissue, and (c) taking into account excretion with the assumption of a "biological half-life" of eleven days, 1 microcurie destroyed per gramme gives a dose of 610r, hence 6 millicuries destroyed in a 70 kilogram man deliver a dose of approximately 50r in an equivalent over-all time of the order of 16 days.* These calculations are only approximate. It has yet to be proved that equal biological effects are produced by equal energy absorption of external gamma radiation and of the radiation from P^{32} ; there are suggestions that the biological effects of the latter are less. Further, in radio-active isotope therapy it is often essential to measure the differential absorption ratio (D.A.R.), i.e., the ratio of the concentration of the radio-active material in a particular tissue to the mean concentration in the body as a whole. The possibility of delivering a therapeutically useful dose of radiation in any particular case can thus be determined with reasonable certainty by measurement of the D.A.R. with tracer doses (20).

"In the clinic at the University of Chicago, it has been customary to treat lymphomas and leukaemias by the administration of small doses (ca. 1 millicurie) once to twice weekly over varying periods, depending upon the response. Polycythæmia rubra vera has been treated by a single intravenous administration of 6 to 8 millicuries. As in roentgen-therapy further treatment is determined by the time of recurrence of disease" (10). It seems that one can treat a typical case of chronic myeloid leukaemia with an initial dose of 2 millicuries of P^{32} , followed by perhaps 4 or 5 doses of 1 mc. at 3- or 4-day intervals, and then doses of 1 mc. weekly until the total white cell count has fallen to 30,000 per c.mm.; then one or two further doses of 1 mc. may be given subsequently at longer intervals. The general clinical picture must obviously be the main guide, as with conventional radiotherapy.

Radiophosphorus has been used in the treatment of patients since 1936. The only disease in which it has been found to give better results than X-ray therapy is *polycythæmia vera*, and it is generally believed to be the treatment of choice in this condition. Different patients vary greatly in their response to the same dose. It usually takes two to three months after the P^{32} for the red-cell count to settle down to the lower level. It is claimed that remissions after P^{32} treatment have lasted up to four years.

In *chronic myeloid and chronic lymphatic leukaemia*, the results and limitations of radiophosphorus therapy appear to be similar to those of X-ray therapy. In these conditions, supplementary X-ray therapy to the spleen or to lymph nodes may be needed. Even in the treatment of chronic myeloid

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leukæmia there appears to be a tendency to rely on X-radiation and to discard radiophosphorus as less safe. In most cases of *lymphosarcoma*, treatment with radiophosphorus is probably less beneficial than with X-rays. The response of *Hodgkin's disease* to P^{32} is very variable and on the whole unsatisfactory. Radiophosphorus is useless in the rare diseases: acute leukæmias, monocytic leukæmia and multiple myelomatosis.

It is important to emphasize that radiophosphorus, used in the form of inorganic phosphate, is of no therapeutic value in cancers generally. I am doubtful if the use of P^{32} as inorganic phosphate will stand the test of time as a therapeutic agent. Probably, selectively concentrated organic compounds containing radio-active isotopes are more promising.

Whenever radiophosphorus is administered internally as inorganic phosphate, its deleterious effects on the normal tissues must be considered, especially on the reproductive organs, bone marrow, and lymphoid tissue, and also, when the expectation of life is considerable, on the kidneys. It is important to recognize that all proliferating cells, normal and malignant, concentrate the radiophosphorus in the process of utilizing inorganic phosphate for the synthesis of important cell constituents, including ribonucleic and thymonucleic acids.

The reality of these possible dangers has been demonstrated histologically by Platt (21) in patients treated with radiophosphorus. The histological changes observed were similar to those produced by external irradiation and striking changes were found in the bone marrow, lymph nodes and spleen. In addition, significant renal changes were observed and "can probably be attributed to the concentration that occurs in the nephron during the process of filtration and re-absorption". "Finally, serious consideration must be given to the changes in the testes and ovaries of patients who are in the reproductive period of life. Observation of these organs confirms the possibility that spermatogenesis and oogenesis may decrease or disappear, with development of sterility, in young persons given radiophosphorus". Genetic injury is probably of less importance.

Another more remote risk from the use of radiophosphorus in the treatment of patients with a long expectation of life is late carcinogenesis, meaning the possibility of induction of leukæmias and osteogenic sarcoma after a latent period, which may be five years as a minimum, but is probably much longer. It is difficult as yet to assess this risk, especially in view of the natural history of polycythæmia vera with its tendency to development of leukæmic states, and probably in many cases the doses of radiation from the radiophosphorus are too small to be dangerous. Nevertheless, in my opinion, it is usually unwise to employ radiophosphorus in the treatment of patients of either sex in the reproductive period of life, and caution is necessary in patients when the expectation of life exceeds five years.

In general, it must be concluded that therapeutic trials of radio-active isotopes should be limited to cancer and allied diseases, including polycythæmia vera. With rare exceptions, radio-isotope therapy should not be used in non-malignant conditions until more evidence is forthcoming. Further, the opinion has been expressed that in the present state of knowledge, radio-active isotopes should in no event be used in the treat-

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satisfactory is *Hodgkin's disease*. It is not justifiable to use it in early cases because X-ray therapy is much more effective and far safer, but in advanced cases, especially when the radioresistant stage has been reached, nitrogen mustard will often produce useful, occasionally dramatic, temporary remissions. The remissions are usually short—often only four to eight weeks, but rarely up to six months. Re-treatment with nitrogen mustard is possible in a few cases, although not within two months. It has been found that previously radioresistant cases have become radiosensitive again after treatment with nitrogen mustard, but whether this applies to cases previously treated with total body radiation is uncertain.

Similar palliative effects, which are often disappointingly brief and on the whole less satisfactory, although still useful, are seen in generalized lymphosarcoma, and have also been observed in chronic lymphatic leukæmia, follicular lymphoblastic reticulosarcoma, and mycosis fungoides (30). Some benefit may be obtained in chronic myeloid leukæmia; acute leukæmias do not respond. There is evidence that nitrogen mustard therapy is of some value in polycythæmia vera, but as yet it is too soon to assess this (10). It is reported that temporary improvement is obtained in some cases of carcinoma of the bronchus, but one cannot be optimistic about the value of nitrogen mustard used alone, or in combination with radiation in this only too common and terrible disease. In cancers generally, the "bis"-nitrogen mustard has no beneficial effect.

With regard to the dose and method of administration of the "bis"-nitrogen mustard, the usual course of treatment recommended consists of four daily intravenous injections, each of 0.1 mgm. of the methyl-bis(beta-chlorethyl)amine hydrochloride per kilogram of body weight. (1 lb. = 0.454 kgm., so that the unit dose for a man of weight 9 st. 8 lb. is 6.1 mgm., say 6 mgm.). I think it is often wiser to give the unit doses on alternate days instead of on consecutive days, and also sometimes to reduce the dose or the number of treatments.

The nitrogen mustard—methyl-bis(beta-chlorethyl)amine hydrochloride—must be given intravenously. Extravasation will produce a quite severe local reaction. Thrombosis of the vein injected may occur occasionally.

The solution must be made up freshly, as follows:—10 c.cm. of sterile saline are injected by means of a 10 c.cm. syringe into the ampoule containing 10 mgm. of the compound, which is an easily soluble white crystalline powder. After dissolving, the calculated volume of solution containing 1 mgm. per c.cm. is drawn up into the syringe. The rest of the solution must be discarded.

These compounds are unstable and the pharmacological effects appear to be due to the formation of a cyclic ethylenimonium cation (22, 31). The solution of nitrogen mustard must be used immediately, and can be injected directly into one of the veins of the arm, but it seems preferable to inject it into a normal saline intravenous drip system already set up and running.

Many of the patients complain of nausea, and some vomit within a few hours after the injection. The nausea and vomiting usually settle down within six hours and seem to be minimized by administration of 20 mgm.

ment of children suffering from non-malignant diseases. I personally would exclude the internal therapeutic use of radio-active isotopes in any conditions in children.

Radio-iodines.—Although the short-lived isotope I^{130} (of half-life 12.6 hours) has been used in some of the pioneer work (12, 15), it appears that the isotope, I^{131} (of half-life 8 days) is the most suitable radio-iodine for therapeutic use. With this latter isotope (I^{131}), 1 microcurie destroyed per gram of tissue delivers a dose of approximately 127r.

Most of the clinical trials of the radio-iodines in the U.S.A. have been carried out in cases of hyperthyroidism (12-17). It is evident that selected cases respond satisfactorily. As yet there is no evidence of risk of carcinogenesis, but insufficient time has as yet elapsed. With the tissue doses given, of the order of 5000r, there is probably little risk of late carcinogenesis, but obviously great caution is necessary. It appears that radio-iodine may have a useful place in the treatment of cases of hyperthyroidism which recur after surgery. Apart from this group of cases, until further information is available, it is probably wise to restrict clinical therapeutic trials of the radio-iodines to the more difficult problem of carcinoma of the thyroid. Only a very small proportion of all cancers of the thyroid retain the function of iodine concentration sufficiently to deliver therapeutically useful doses with radio-iodine. There are extremely rare cases of carcinoma of the thyroid, in which functional secretion is a striking feature of both the primary and metastases, and dramatic results can be obtained by radio-iodine therapy (15). Unfortunately, these interesting and widely discussed cases are uncommon, and there appears to be only a limited field for clinical trials of the therapeutic possibilities of the radio-iodines. "The vast majority of thyroid cancers are totally unaffected by radio-iodine" (9).

RADIOMIMETIC CHEMOTHERAPEUTIC AGENTS

Nitrogen mustards.—The therapeutic possibilities of this group of compounds were recognized in 1942 by Gilman and Philips (22) in the course of chemical warfare research, and a number of reports of clinical trials appeared in 1946 (23-25). The work was based on the pharmacological resemblance, including mitotic inhibition and damage to proliferating cells and lymphocytes, of the mustard-gas series of chemical warfare agents. It was supported by the important discovery in 1943 by Auerbach that these chemicals produce gene mutations and chromosome rearrangements similar to those induced by X-rays (see Darlington and Koller, 26). There are many recent reports of further clinical trials (1, 2, 10, 27, 28, 29).

The nitrogen mustard used most widely has been the *bis* compound, methyl-*bis*(*beta*-chloroethyl)amine hydrochloride. This agent is highly toxic and must be employed with the greatest care. Although it will probably be superseded, it is generally recognized to have a definite, although limited, palliative therapeutic value. The condition in which the response is most

satisfactory is *Hodgkin's disease*. It is not justifiable to use it in early cases because X-ray therapy is much more effective and far safer, but in advanced cases, especially when the radioresistant stage has been reached, nitrogen mustard will often produce useful, occasionally dramatic, temporary remissions. The remissions are usually short—often only four to eight weeks, but rarely up to six months. Re-treatment with nitrogen mustard is possible in a few cases, although not within two months. It has been found that previously radioresistant cases have become radiosensitive again after treatment with nitrogen mustard, but whether this applies to cases previously treated with total body radiation is uncertain.

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of pyridoxine, three times daily by mouth. There is usually anorexia during the course of injections.

Far more serious is the risk of damage to the bone marrow and lymphoid tissue. It is essential to have frequent blood counts, e.g., on alternate days during the injections and twice weekly for three weeks afterwards, then weekly for several weeks. It is desirable to examine the sternal marrow before starting treatment. In some cases it has been necessary to give several blood transfusions after the nitrogen mustard treatment.

The similarity of the effects of the nitrogen mustard to those of X-radiation is striking; probably a dose of 0.1 mgm. per kgm. corresponds to between 25 and 50 of total body X-radiation.

Urethane.—Urethane (ethyl carbamate), was found to inhibit the growth of various animal tumours (Haddow and Sexton, 32). This was followed by a clinical trial in which the radiomimetic action of urethane in leukæmia was discovered (1, 33). Further clinical trials have been reported (1, 2, 34, 35, 36). It is yet too soon to judge the therapeutic value of urethane, but there is no doubt that it produces satisfactory remissions in some cases of chronic myeloid and of chronic lymphatic leukæmia. It is probably more effective in the former type. "It now appears that while urethane has almost certainly no practical advantages over X-ray therapy, the degree of response . . . may be very similar in the two cases" (37, p.50). Craver (29) considers that "urethane may produce remission of chronic leukæmia, usually only after administration for a few to several weeks, and in only about one-fourth to one-third of the cases".

The dose of urethane is 3 to 4 gm. per day, usually by mouth, i.e. 1 gm., either in a mixture or in capsules, three or preferably four times daily. Nausea occurs in some cases, but in these the drug can be given rectally in saline or even intravenously. The length of time of administration depends upon the clinical and hæmatological progress and is often three to five weeks. Urethane is not very toxic (but see 34) and promises to be a useful aid in the treatment of chronic leukæmias. It does not appear to be useful in cancers generally. Occasionally, although not generally, it is beneficial in multiple myelomatosis (38).

HORMONES AND HORMONE-LIKE CHEMOTHERAPEUTIC AGENTS

Cancer of the prostate.—The only reasonably successful chemotherapy yet available for cancer is the use of synthetic œstrogens, in particular stilbœstrol, in the treatment of cancer of the prostate. There is not the slightest doubt as to its great palliative value even in advanced cases with metastases in the bones and lungs.

"The use of stilbœstrol appears to give a significant increase in the expectation of life, and in particular to reduce the alarming mortality of the first year" (1).

It has yet to be proved whether it is possible to use stilbœstrol to control cases of cancer of the prostate permanently or for long periods.

It is well known that the anti-androgenic treatment of cancer of the prostate was introduced by Huggins in 1941 (see 38, 2, 1). Stilbæstrol had been introduced by Dodds *et al.* (40) in 1938, and Huggins and his collaborators used it in cancer of the prostate with strikingly beneficial results, which have been confirmed throughout the world. It is worthy of comment that Huggins (39) is still of the opinion that "for most patients, it is less efficient than castration". Nevertheless, the objections to the latter are such that it is seldom used, at least in this country.

Cancer of the prostate is still a surgical disease. It is estimated that although only a few per cent. of cases are seen sufficiently early for radical prostatectomy, about 90 per cent. of the cases have some degree of urinary obstruction requiring surgery. The importance of histological confirmation must also be mentioned.

A useful plan of dosage of stilbæstrol is to start with a 1 mgm. tablet t.d.s. by mouth, and increase the dose daily by 1 mgm. t.d.s. up to 5 mgm. t.d.s., and then increase in some cases further to 5 mgm. four times daily. The serum acid phosphatase should always be estimated before giving stilbæstrol and if raised, as when osseous metastases are present, its fall after stilbæstrol therapy is an index of response and a general, although not invariably reliable, guide to the determination of the maintenance dose. After continuing with 15-20 mgm. daily for weeks or months, according to the clinical response, the dose is gradually reduced to the maintenance level, which in some cases remains at 10-15 mgm. daily. It is of vital importance not to discontinue the stilbæstrol under any conditions. It must be impressed upon the patient that he has to continue to take it for the rest of his life.

In a few cases, stilbæstrol produces nausea or vomiting. Dienæstrol can be substituted but is probably less effective. Alternatively, and often preferably, the stilbæstrol can be given intramuscularly. I use a solution containing 50 mgm. of stilbæstrol in 1 c.cm. of peanut oil. Pyridoxine appears to reduce the nausea in some cases.

The main side-effects of stilbæstrol therapy are testicular atrophy and impotence, which are inevitable; enlargement of the breasts, and pigmentation of the nipples, surgical scars and mid-scrotal line occurs in many cases. None of these effects is an indication for discontinuing the stilbæstrol.

Probably less than ten per cent. of cases fail to respond initially to stilbæstrol. To produce an initial response it seems to be rare to require doses higher than those suggested. The initial beneficial effects are often dramatic, especially with metastases in the bones, with pathological fractures, and with pulmonary metastases. There appears to be a useful place for the combination of palliative radiotherapy with stilbæstrol, especially in the treatment of the skeletal metastases. With stilbæstrol, as so frequently is the case with other agents used to treat cancer, the effects are not permanent, and in most cases, after a variable interval of time which may be several years, symptoms recur. Increase of the daily dose of stilbæstrol often produces a temporary improvement, and although occasionally the remission may last for perhaps a year, usually the prognosis is poor. In some of these stilbæstrol-resistant cases X-ray therapy is still of palliative value. In these

relapses, often the metastases alone progress while the prostate itself remains atrophic.

Cancer of the breast: (a) Stilbæstrol.—The success of stilbæstrol in the treatment of carcinoma of the prostate was followed by largely empirical clinical trials of synthetic œstrogens in various types of advanced malignant disease. Limited success has been obtained in some cases of advanced cancer of the breast (41, 42). In a discussion of preliminary results (43) without controls, it was reported that of 168 cases, 41 were "improved" and six showed "spectacular improvement". Patients over the age of sixty respond much more often than do younger patients. The beneficial effects are seen principally when the soft tissues, and not the bones, are involved. There is no evidence that stilbæstrol prevents the development of metastases. It is not yet possible to assess the value of stilbæstrol in advanced cancer of the breast, but the beneficial results are, certainly only palliative and temporary. There is no adequate information as to dosage.

It seems wise in general to employ rather high doses, such as 25-50 mgm. and even occasionally 100 mgm., daily, given preferably intramuscularly, but good palliative results are sometimes seen with much smaller doses or with doses such as 25 mgm. repeated once a fortnight.

There is great individual variation in the response of the patients to stilbæstrol. Of the undesirable side-effects, nausea and vomiting are frequent and appear to be helped by pyridoxine, 20 mgm. b.d. or t.d.s.; the most important is the induction of "menstruation" or metrorrhagia, which is erratic in its occurrence and occasionally severe, but concerning the possibility of which the patient should always be warned. Rarely, even with small doses, there is mild mental confusion which disappears after stopping the stilbæstrol.

Stilbæstrol and X-radiation are often used in conjunction, and especially in the case of skeletal metastases small doses of radiation are frequently of great palliative value.

(b) Testosterone.—Beneficial effects of large doses of testosterone have been described in some cases of advanced cancer of the breast, especially with skeletal metastases (44-48). Testosterone can be used for patients of any age. The usual dose of testosterone propionate in the treatment of skeletal metastases from cancer of the breast is 25 mgm. daily by intramuscular injection, or 50 mgm. on alternate days. Useful results have been reported with total doses of 500 mgm., but doses as large as 4000 mgm. in 100 days have been given. These doses will produce at least minor signs of virilism and of course temporary amenorrhœa. It is said that in some patients there is a danger of severe hypercalcæmia, so that estimations of the serum calcium should be done.

The most important beneficial effects reported are relief of pain and recalcification of osteolytic metastases. However, these beneficial results are produced in only a small proportion, perhaps 15 per cent. of the patients

treated, and are of course only temporary. Some patients are made worse by testosterone. It is yet too soon to assess the therapeutic value of this interesting development.

MISCELLANEOUS CHEMOTHERAPEUTIC AGENTS

Arsenic.—Inorganic arsenic, in the form of Fowler's solution (potassium arsenite), still has a useful though minor place in the treatment of chronic myeloid leukæmia. It is also given in chronic lymphatic leukæmia and Hodgkin's disease, but in these conditions it usually appears to be considerably less effective. It is said that a leukæmia responding dramatically to arsenic should be suspected of being monocytic in type (49). Arsenite will produce a remission in probably most cases of chronic myeloid leukæmia in the early stages, but of greater importance is the possibility of producing a remission in some cases which have reached the radio-resistant stage.

The method of administration of Fowler's solution (Liq. arsenicalis) generally used is as follows:—The initial dose is 3 minims t.d.s., either immediately after or with meals. On consecutive days, each dose is increased by 1 minim up to 10-12 minims t.d.s., or even higher up to tolerance. This level is continued for seven days, or as suggested by the blood picture, and then each dose is reduced by 1 minim each day, until a maintenance dose of 5 to 8 minims t.d.s. is reached. This must be continued indefinitely and mild toxic symptoms should be disregarded.

Arsenic is the oldest chemotherapeutic agent for leukæmia which has stood the test of time. It was first used by Lissauer in 1865, and its use was revived in 1931-2 (50). Radio-arsenic has recently been used in clinical trials in leukæmias.

Stilbamidine and pentamidine.—An interesting recent development, sufficiently convincing to justify clinical trials, is the therapeutic application of stilbamidine (4,4'-diamidino-stilbene) and pentamidine (4,4'-[pentamethylene-dioxy]dibenzamidine), combined with a diet low in animal protein, in multiple myelomatosis, reported by Snapper (51, 52). By no means all cases respond, but in some the effects are dramatic and in particular there is a striking relief of pain. It must be emphasized that the treatment is palliative, merely checking the progress of the disease, and that the beneficial effects are temporary, with relapses in some cases after six months. There is great individual variation in the response of different cases; some respond to either stilbamidine, pentamidine, urethane (38), or X-radiation, and not appreciably to any of the others.

Most of the trials have been carried out with stilbamidine, but pentamidine should probably be examined more widely to avoid the possibility of delayed side-effects. So far, there is no evidence that stilbamidine alone or in combination with X-radiation is therapeutically effective in any of the common types of advanced cancer.

Stilbamidine is usually administered intravenously, but appears to be satisfactory when given intramuscularly in 5 c.cm. of 2 per cent. novocain. For intravenous

relapses, often the metastases alone progress while the prostate itself remains atrophic.

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injection, the stilbamidine (di-isethionate) is dissolved in 10 c.cm. of distilled water. The solution should not be autoclaved. The dosage is as follows:—A first injection of 50 mgm. is given, followed two days later by 100 mgm. Thereafter, 150 mgm. is given, usually on every other day, but in some cases daily. It is probably wiser to continue to a total dose of 4 to 5 gm., but good palliative results have been obtained after 2 gm. A few patients complain of sweating and dizziness after the injection, and this appears to be prevented by giving 1/200 to 1/150 grain of atropine sulphate before the stilbamidine. Most of the patients lose their appetites and develop a curious grey cyanosis at the end of the course of injections; these effects disappear rapidly when the injections are stopped. The relief of pain often begins after the third or fourth injection, and is sometimes so rapid that, to avoid the risk of new pathological fractures, caution is necessary in allowing the patients to get up. It is said that no benefit is obtained when the treatment is accompanied by a diet high in protein.

There is one rather common delayed toxic side-effect of stilbamidine treatment, namely, the "dissociated trigeminal anæsthesia", which is well recognized (53-56) and which, although usually trivial, is a serious problem in a few cases.

Snapper (51) observed it in four out of twenty patients. Napier (56) and Hargreaves (57) observed it much more frequently. The neuropathy may appear about three to four months after the end of the course of injections; it usually lasts several months and has a tendency to spontaneous recovery. There is loss of sensation to light touch only, with paraesthesiae, in the trigeminal areas.

This side-effect is probably not a serious drawback to the use of stilbamidine in the palliative treatment of multiple myelomatosis, but it is evident that the therapeutic value of pentamidine and other amidines, which do not show this toxic effect, must be explored. Snapper (51), for instance, has said that "pentamidine was given every other day in intramuscular injections of 100 mgm. dissolved in 5 c.cm. of distilled water. The total dosage given varied between 2 and 3 grams".

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pain in the face, especially when bilateral should, in the absence of positive signs, suggest a psychogenic origin. Usually careful history taking will bring out points in support of or against this diagnosis.

TREATMENT

As an initial step in the treatment of trigeminal neuralgia, a careful dental overhaul should be undertaken, but unless some definite pathology is found extractions should not be carried out. The antrum should be X-rayed, and washed out in doubtful cases. Attention to general health is important. The patient should be informed of the nature of the complaint, particular stress being placed on the fact that long intervals may occur between attacks. Assurance should be given that drugs are available that can mitigate the pain.

Medicinal treatment.—This must be given a proper trial in every case; alcohol injection or operation should only be considered if the interval between attacks is short and if other measures have failed. These procedures should not be discussed with the patient in the early stages of the complaint. In mild cases the following mixture may relieve pain:—

R Potassium bromide	10 grains (0.65 gm.)
Tincture of gelsemium	10 minims (0.6 c.cm.)
Phenazone	7 grains (0.45 gm.)
Water	$\frac{1}{2}$ oz. (14.2 c.cm.)
Sig. $\frac{1}{2}$ oz. (14.2 c.cm.) three times daily.	

When the pain is more severe a powder containing aspirin, 10 grains (0.65 gm.); pyramidon, 10 grains (0.65 gm.); and heroin, $\frac{1}{10}$ grain (6.5 mgm.), may occasionally be given, but opium derivatives should not be used as a routine. Of the newer analgesics, physeptone (Burroughs Wellcome) should prove the best: 1 to 2 tablets (5 mgm.) three times daily may be given for a short period. In between the attacks of pain phenobarbitone, $\frac{1}{2}$ grain (32 mgm.) t.d.s., is sometimes indicated.

Alcohol injection.—An injection, whether of one of the branches of the nerve or of the ganglion, seldom gives relief for longer than two years; the patient should be informed of this fact and of the numbness of the face which will follow. A maxillary nerve injection may be made either at the infra-orbital foramen where the nerve emerges, or at the foramen rotundum. In the case of the mandibular division, the nerve is injected at the foramen ovale, either by the horizontal lateral approach or an ascending anterior approach (Harris). Finally, when more than one division is affected, injection of the Gasserian ganglion may be carried out by the ascending anterior approach, as used for injection of the third division. It must be emphasized that in the hands of the inexperienced, complications may readily arise from unsuccessful attempts to inject the ganglion.

Surgical treatment.—When carried out by an experienced neurosurgeon operation for the relief of trigeminal neuralgia is a safe procedure. In deciding between an alcohol injection and operation, the patient's age, state of general health, and the availability of a reliable neurosurgeon are among the factors that should be considered. The operation usually employed is an extradural section of the sensory root of the fifth nerve behind the Gasserian ganglion. Pain is relieved permanently. Precautions against a keratitis must be taken, both following operation and alcohol injection.

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REVISION CORNER

TRIGEMINAL NEURALGIA (*Tic douloureux*)

TRIGEMINAL neuralgia remains a clinical entity of unknown origin. Its occasional association with dental infection, and more rarely with infection of the antrum, and the fact that, in the great majority of cases, the pain is first felt in either the second or third divisions of the fifth nerve, tend to support the view that a neuritis of the terminal filaments of the fifth nerve is the primary cause of the condition. However, there remains unexplained the reason why only a small percentage of people with infection of the jaw become victims of this condition. In 2 per cent. of cases there is a family history.

SYMPTOMATOLOGY

The essential feature of trigeminal neuralgia is the paroxysmal character of the pain. A sudden, sharp, excruciating stab or wave of burning pain is felt in the lower jaw or upper lip, or in the cheek or, more rarely, in the tongue. The pain persists for a few seconds and then suddenly ceases. The attacks are brought on by touching a so-called "trigger zone", e.g. part of the lip or cheek, but other precipitating factors are common, such as talking, eating, a current of cold air or a sudden noise. The pain may be so severe as to result in a reflex spasm of the face on the affected side (*tic douloureux*). Attacks may recur during one or more days, causing a degree of mental stress that is rarely exceeded by any other type of painful disease. A free period of months or even years may follow the first attack, but the intervals between the attacks become shorter and their duration longer, leading to a state of anxiety and depression, so severe in some cases that suicide is contemplated. No sensory, reflex or motor changes are found within the distribution of the trigeminal nerve unless the patient has had a previous alcohol injection.

DIFFERENTIAL DIAGNOSIS

When a patient complains of pain in the distribution of the first division of the fifth nerve, trigeminal neuralgia is seldom the cause unless there is a clear history of the condition having previously affected one of the lower branches. Pain due to an infected antrum is felt within the territory of the second division; it is a constant pain and is usually associated with local tenderness and sometimes swelling. Pain in the second or third divisions of the fifth nerve is commonly caused by dental caries or by an apical infection. The pain is more persistent and does not have the short, sharp, paroxysmal character of trigeminal neuralgia. Tapping the teeth with a metal probe may reveal the cause, or X-ray examination may be necessary. A numbness in the distribution of the fifth nerve with or without pain should suggest an organic condition, such as a tumour of the fifth nerve or of the Gasserian ganglion. Numbness over the cheek is one of the earliest neurological signs of a nasopharyngeal tumour or of carcinoma of the ethmoid. Occasionally, trigeminal neuralgia may be associated with disseminated sclerosis. Individuals with a migrainous family history may have attacks of severe pain in the region of the eye, either referred behind the eyeball or to one or other canthus. The pain may radiate down into the cheek and upwards into the forehead. Such attacks of *migrainous neuralgia* may last for a few days or a few weeks, with free periods. The precipitating factors that are so characteristic of trigeminal neuralgia do not occur in this condition. Ergotamine tartrate and phenobarbitone may give relief. If this treatment fails, injection of the inner part of the Gasserian ganglion, with resultant anaesthesia in the first and second divisions of the fifth nerve, may prove successful (Harris). Lastly, constant discomfort or actual

examples may usually be diagnosed from the evidence of obvious disease elsewhere in the body. For rational treatment, separation of the three major causes of "chronic dysentery" is essential, and therefore something must be said of bacillary and amœbic infections although they are not examples of "non-specific" disease.

Chronic bacillary dysentery.—This relatively uncommon disorder is hardly seen outside endemic areas and thus in this country occurs only in those who have returned from overseas. It is seen in patients whose acute bacillary infection has never really cleared up and follows directly upon an acute attack. Diagnosis depends upon observing the nature of the stool, the hyperæmia and ulceration of the mucosa on proctoscopy, and the identification of *B. dysenteriae* (usually *Shiga*) in the stool. Relapsing dysentery is never bacillary. Patients with chronic bacillary dysentery are emaciated and anæmic. Apart from the administration of sulphonamide drugs, an easily assimilable high protein diet free from irritant residua is necessary, and sometimes blood transfusion is needed. As failure to respond to treatment suggests the possibility of concomitant amœbic infection, even if amœbæ are not discovered in the stools, the effect of giving emetine should be observed in recalcitrant cases. Failure to respond to treatment in cases which, although resembling bacillary dysentery fail to show the presence of *B. dysenteriae* and which are known not to be amœbic, suggests that the true diagnosis is ulcerative colitis, a disease not restricted to temperate climates.

Chronic amœbic dysentery.—This disorder may follow on an acute attack or may recur after an interval of apparent health. The stools much less commonly contain bright red blood, and, whilst bacillary dysentery attacks the rectum always and ulcerative colitis nearly always does so, amœbic disease is often limited to the ascending colon. The stool then is unformed and homogenous. Sigmoidoscopy may reveal typical amœbic ulceration; amœbæ or amœbic cysts may be discovered in the stools. Nevertheless, amœbic dysentery must sometimes be diagnosed in the absence of amœbæ in the stools or of specific ulcers in the rectum. But because accurate diagnosis of chronic amœbic dysentery is of the greatest importance to the patient (it involves a long course of treatment if diagnosed, and the dangers of relapse and metastatic infection in the liver if not) care must be taken to distinguish the malady from "post-dysenteric diarrhœa", a common functional disorder of the bowel which is discussed below. True chronic amœbic infection is characterized by a history of an acute attack, perhaps incompletely treated, and subsequent relapse. The patient's complexion is often muddy and there may be tenderness in the right iliac fossa or over the colon generally. With an adequate history and adequate objective signs, even when there has been failure to demonstrate amœbæ, the patient should be recommended a preliminary course of penicillin followed by emetine, quinoxyl and carbasone; this will take several weeks to give. Although the history is similar in post-dysenteric diarrhœa, there are no abnormal physical signs.

Chronic ulcerative colitis.—This disorder presents few difficulties in diagnosis; because the rectum is almost always involved, sigmoidoscopy shows a velvety bleeding mucosa with rather superficial ulceration. Many patients pass fairly normal stools but bleed profusely; others show severe diarrhœa without the loss of very much blood. In all types, however, sigmoidoscopy and bacterial examination of the stools, to exclude infective dysentery, leave the diagnosis in little doubt. The treatment of this condition has been a subject of discussion and of innovation since the disease was first described by Gull nearly a century ago. Perhaps in no disease has chemotherapy been so consistently disappointing, and recent hopes that sulphaguanidine, penicillin, dried chitterlings or folic acid might prove useful remain unsubstantiated. The spontaneous remissions of the disease and frequently the great length of its natural history render assessment of treatment difficult. It is doubtful whether any specific treatment at all is of value, and no worse results are obtained by putting the patient to bed, treating his anæmia with iron and blood

THE TREATMENT OF NON-SPECIFIC DIARRHŒA

DIARRHŒA is a symptom of many diseases, and in the account which follows, those maladies alone are described in which diarrhœa is the presenting or one of the most important symptoms, and which do not depend upon infection with specific micro-organisms.

The treatment of diarrhœa raises many difficulties, but treatment of the symptom alone without due regard for the underlying cause will usually result in failure. It is essential at the start to be sure that the patient is in fact suffering from diarrhœa, that is, from the frequent passage of abnormally soft or fluid stools, and not from frequent calls to stool when small quantities of blood or pus or mucus, perhaps with the addition of small quantities of faecal matter, alone are produced. Such spurious diarrhœa usually attends gross abnormalities of the lower bowel; in particular, new growths of the rectum and of the sigmoid colon. Occasionally, patients with chronic constipation who are accustomed to take increasing doses of irritative purgatives, complain of frequent calls to stool but pass only mucus. Rectal examination will usually reveal the presence of hard faecal masses and the true diagnosis.

Whatever be the basis of diarrhœa, the immediate cause is the passage into the rectum of unusually frequent and unusually bulky, or of unusually irritant, material; the consequent distension or irritation of the rectum causes a desire to defæcate. An abnormally irritable state of the distal part of the colon or of the rectum from inflammation or new growth similarly causes diarrhœa.

The normal healthy colon receives fluid faecal material from the small intestine. This accumulates in the ascending colon, and usually once or twice a day, and often after a meal in response to the gastro-colic reflex, is emptied into the rectum by a single mass peristaltic movement. The rectum is distended and the desire to go to stool is experienced. This normal behaviour can be upset either by unusually large quantities of fluid or by abnormally irritant fluid reaching the ascending colon from the ileum, or from an abnormally irritable state of the colon failing to allow stasis and water absorption. It follows that faecal material is passed too quickly into the rectum. There are two main types of diarrhœa: that depending upon abnormality of the small intestine, and that depending upon abnormality of the large intestine. Chronic small intestine diarrhœa and large intestine diarrhœa may often be distinguished by the gross appearance of the stool, and as the latter is the more common it will be considered first.

LARGE INTESTINE DIARRHŒA

The stools in cases of large intestine diarrhœa usually show some evidence of the dehydrating effect of the colonic mucosa so that the stool is rarely homogenous; there are often some at least partly formed elements and, at times, the patient may pass a normal stool. These features are more marked when the inflammatory or irritant process is limited to the distal part of the large bowel. Thus, in the presence of an ulcerating growth of the sigmoid colon, a mixture of fæces, blood and mucus may at times be passed. Similarly, in cases of ulcerative colitis when the disease is limited to the lower part of the colon, as it often is, formed faecal elements are often seen. When the whole of the colon is the seat of disease, then the stool more closely resembles that seen in "small intestine diarrhœa", as it also does in cases of gastro-colic fistula.

The causes of true chronic diarrhœa arising in the large bowel are few and almost always depend upon chronic inflammatory ulceration or upon malignant ulceration. In these cases blood is usually seen in the stool, at least from time to time. Chronic inflammatory ulceration of the colon may be due to chronic dysentery, either *amœbic* or *bacillary*, or, much more commonly in the United Kingdom, is of unknown cause, when the disorder is termed *ulcerative colitis*. Tuberculosis, uræmia and polyarteritis nodosa also give rise to ulceration of the large bowel, but such

important in the treatment of diarrhœa which does not primarily depend upon this defect of secretion.

Nervous diarrhœa.—Although diarrhœa from nervous causes is usually acute in form and its cause evident to the patient, in chronic anxiety states the habit may become established. Diarrhœa is not uncommon in hyperthyroidism and is occasionally the presenting symptom.

POSTDYSENTERIC DIARRHŒA

It is common in patients who have suffered from long-standing tropical diarrhœa from any cause, and particularly after amœbic dysentery, for the stools to remain unformed and to number perhaps four or five a day. The postprandial tendency of the diarrhœa is marked and exacerbations follow dietetic and particularly alcoholic excess. The patients are usually otherwise in good health, but great care must be taken to distinguish the condition from chronic intestinal amœbiasis.

These cases are examples of an exaggerated gastro-colic reflex and abnormal irritability of the bowel. So long as no other cause for the diarrhœa is present, treatment is symptomatic and is simple and efficacious. The nature of the disorder must be explained to the patient; he must be told of the necessity to re-educate his bowels; achlorhydria must be corrected if present, and intestinal activity damped down by the use of codeine and a belladonna mixture. Abstinence from alcohol and the use of a non-irritant diet are also necessary. The patient can gradually be weaned from his medicines after a week or two but an occasional dose of codeine will be necessary for two or three months, when a normal diet may gradually be resumed.

CONCLUSION

Chronic looseness of the bowels is often symptomatic of serious disease and exact diagnosis must always precede treatment. Suppression of the symptom alone is dangerous. Full investigation may be necessary to discover the cause, but when it is determined, if efficacious treatment is available, the lines it should follow usually present but few difficulties.

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It is natural to turn to surgery when the failures of conservative treatment are so commonly seen. The only immediate operation of value in the acute stage of ulcerative colitis (apart from the suture of a perforated colon, a rare complication) is that of ileostomy. As soon as the flow of fæces through the colon stops, the bleeding and discharges are reduced and the patient regains his general health, often with great rapidity. The operation hitherto has usually been reserved for the more desperate cases because, whatever is hoped for at the time, ileostomy generally proves to be permanent. Closure of the ileostomy is followed by relapse. It is logical therefore, until more is known about the cause of this disease and some rational treatment discovered, to consider colectomy at an interval of some months at least after the ileostomy is established, in the hope that ileo-rectostomy may be undertaken later. Hurst and Ogilvie began to treat patients with such a plan in mind during the years before the war. It would be easier to carry out this method in the less severe case, but one, nevertheless, of which it was thought that the ultimate prognosis was bad.

SMALL INTESTINE DIARRHŒA

Acute diarrhœa due to irritation of the small intestine frequently depends upon infection with organisms of the food-poisoning group, with *B. dysenteriæ* Sonne and with *B. typhosus*; as such they do not concern us here. Acute small intestine diarrhœa may also follow an unusual diet, alcoholic excess, or specific or allergic sensitivity to certain foods. The treatment is obvious.

Chronic small intestine diarrhœa may be due to chronic inflammation of the small bowel; this occurs in tuberculous enteritis and in those cases of ulcerative colitis in which the process spreads into the ileum. Diarrhœa also occurs from irritation of the small intestine by the presence of abnormal chemical constituents of the chyme, and from certain nervous factors; these are discussed below.

Sprue and celiac disease.—Sprue may give rise to a chronic wasting diarrhœa. The cause lies in failure of absorption of fat from the small intestine, largely as fatty acids, which form soaps and irritate the bowel. The stools are frequent, usually of the consistency of porridge, and they are pale, bulky, offensive and greasy. No elaborate assay is necessary to show the excess of fatty acid, for the acicular crystals with an excess of fat globules can be seen under the microscope. Similar disturbances of absorption occur in non-tropical sprue, in celiac disease and in rare cases of lacteal obstruction from tuberculous or malignant disease. The classical treatment of sprue and allied conditions consists of the withdrawal of fat from the diet, and the administration of large quantities of some of the more nutritious fruits. A diet of bananas may be very effective; others have recommended large quantities of strawberries if the disease should happily coincide with the season. Folic acid has been found to be of considerable value in the tropical cases in which there is an associated megalocytic anæmia, but of less value in non-tropical sprue and in celiac disease in children. It is interesting that the Chinese have used liver soup in the treatment of sprue for many centuries.

Achlorhydria.—Lack of acid in the gastric juice may be a cause of chronic diarrhœa which is rarely severe. If a test meal shows an excess of mucus in the specimens, daily gastric lavage with a dilute solution of hydrogen peroxide for a week or two may bring back the acid. In true achylia, however, and in those cases which do not respond to lavage, substitution therapy is necessary; 60 minims (3.6 c.cm.) of dilute hydrochloric acid is taken in a sweetened fruit drink with the main meals. Achlorhydria tends to make diarrhœa from other causes worse; its correction therefore is

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Symptomless mastoiditis was not unknown before 1935, but it is much more common since the era of chemotherapy. The development of this condition usually, but by no means always, means that treatment has started too late, finished too early, and that dosage has been inadequate. Suspicion should always be aroused if discharge persists into the third week, whilst if in addition deafness is a marked feature the onset of mastoiditis is probable. The doctor who appreciates that symptomless mastoiditis is a reality and is prepared to redouble his vigilance during and after the third week, need not hesitate to use sulphonamides according to the well-established rules. Patients first seen when the ear has been discharging for a week or more should not be given sulphonamides with the hope that a "threatened mastoid" can thus be aborted; it is far too late for chemotherapy to be effective, and masking of symptoms is at this stage unavoidable.

W. I. DAGGETT, M.B., F.R.C.S.

The Treatment of Otitis Externa

QUERY.—A woman aged twenty-six years has had bilateral otitis externa for six months. Intermittently there is considerable pain and discharge, the latter being clear or purulent. When purulent, it is foul-smelling. Bacteriological examination shows *Staph. aureus* and coliform organisms in both ears. Mist. spiritus, ichthyol and glycerin, and flavine have all been tried at different times without success. The ears have been regularly swabbed clean daily.

REPLY.—In this answer it is presumed that there is no otitis media underlying the otitis externa. Otitis externa is often associated with a seborrhœic scalp and will not clear up if the scalp remains untreated. If therefore the scalp is greasy the hair should be washed at least twice a week with a spirit shampoo and no grease put on the hair. The essential feature in the treatment of the ears themselves is adequate cleaning. The ears should be syringed with normal saline to start with, and all debris, wax and epithelial scales removed. The ears must then be thoroughly dried, particular attention being paid to the anterior meatal recess. If the lesion is excematous, aluminium acetate should be used as initial treatment. A wick of $\frac{1}{2}$ -inch ribbon gauze is moistened in 8 per cent. aluminium acetate and packed lightly into each meatus. Three times daily the wicks should be moistened with the aluminium acetate solution. After forty-eight hours the wicks are removed and the same solution used as drops once daily for the rest of the week. Dilute ointment of mercuric nitrate, 1 part, and almond oil, 7 parts, is then used as ear drops once daily for a week or two until the ears appear normal. If

the ears are sore after syringing the mercuric nitrate drops may be used at once, omitting the aluminium acetate. These patients are often of a nervous temperament and cure in these cases is helped by giving phenobarbitone, $\frac{1}{2}$ grain (11 mgm.), twice daily for a few weeks. In general penicillin and sulphonamides are not helpful in the treatment of otitis externa.

GEOFFREY BATEMAN, M.B., F.R.C.S.

Acne Rosacea

QUERY.—A female patient, aged sixty years has redness and thickening of the integument of her nose of eight years' duration. The diagnosis is between acne rosacea and lupus erythematosus. She has had treatment with sulphathiazole, stilbæstrol and ultra-violet light.

REPLY.—A diagnosis of rosacea would appear more likely than lupus erythematosus, as there would probably be scarring in the latter condition after eight years. Any variation in the degree of redness at different times, or a tendency to flushing of the face, would further suggest rosacea. It should respond to application of 2 per cent. sulphur and 2 per cent. salicylic acid ointment, together with fractional doses of X-rays, say, 50r weekly at low kv for four to five weeks. Dilute hydrochloric acid, 30 minims (1.8 c.cm.) in a tumbler of water at meals, can help, and riboflavine 3 mgm. t.d.s. Physical factors causing reddening of the face should be avoided and emotional factors dealt with by explanation and sedation. Artificial sunlight treatment is contraindicated.

GEOFFREY HODGSON, M.B.E., M.D.

Rheumatoid Arthritis, Psoriasis and Amenorrhœa

QUERY.—A female patient aged twenty-six, unmarried, contracted rheumatoid arthritis about five years ago. Either shortly before or after this, widespread psoriasis made its appearance. Both these conditions are acute to-day in spite of prolonged hospital treatment with gold injections and routine treatment for the psoriasis. The teeth and throat have been investigated for septic foci without result. About four months ago she had menorrhagia with subsequent amenorrhœa until last week, when menstruation reappeared normally. She now tells me that this last condition occurred with the onset of the other two and at intervals since then. What relation, if any, could exist between these three conditions?

REPLY.—The question as to a connexion between psoriasis and rheumatoid arthritis is constantly being raised from different angles. Some think that there is no etiological connexion between the two and that they merely

appear in the same patient so often because they are both common conditions. Others think there is a true psoriatic arthropathy. The facts which are actually known seem to be as follows—Bauer, *et al.* (1941) found that 23 out of 26 cases of psoriasis with arthritis suffered from the rheumatoid type. In my own series of 254 cases of rheumatoid arthritis, psoriasis occurred 8 times, that is, in 3.1 per cent. Of the patients who suffer from psoriasis about 1 per cent. also have rheumatoid arthritis. The only clinical peculiarity of psoriatic arthropathy is the involvement of the terminal joints and the nails, especially in the foot. As is well known, rheumatoid arthritis in its usual form seldom attacks the terminal joints. The pathology of rheumatoid arthritis and that associated with psoriasis appears to be the same. With regard to the menorrhagia followed by amenorrhœa this is not at all an unusual sequence of events in rheumatoid arthritis, which is a constitutional disease with a pronounced bias for the female sex and in its most classic form involves women of child-bearing age. It is only natural that, in this condition as in many other constitutional diseases, amenorrhœa should occasionally be found. The recent description (Yeoman and Wilson, 1947) of amyloid disease in connexion with rheumatoid arthritis throws an added light on the modern conception of the character of the disease. There is no figure available of the incidence of amenorrhœa, but past experience seems to indicate that it occurs in about the same proportion of cases as in pulmonary tuberculosis. It seems clear then, from these observations, that rheumatoid arthritis may be the condition which holds the other two together, but that there is still some doubt as to whether the so-called psoriatic arthropathy is a coincidence or a specific syndrome. My own personal view is that the two conditions are coincidental.

ERNEST FLETCHER, M.D., M.R.C.P.

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Yeoman, W., Wilson, J. V. (1947) *Brit. med. J.*, ii, 483.

Bleeding During Early Pregnancy

QUERY.—A primipara, aged twenty-two, frail and neurotic (going in to hysterical fits at times), is in the 19th week of pregnancy. She started bleeding per uterus at the beginning of the 12th week. It began as a small quantity (1 in. by 3 in. on a daper) and increased to profuseness (diapers had to be changed five to six times a day) by the beginning of the 15th week. But the os was still closed and the patient was very keen on having a child. She was not prepared for a curettage. Hence the risk was taken, and treatment was continued leuto-

cyclin, 5 mgm., twice a week, ephyllin tablets, 2 daily, calcium gluconate 10 per cent., 10 c cm., with vitamin C, 500 mgm., every 3rd day. Bleeding stopped after a week, but still the discharge is seen (slight) on and off for the last week, after a complete cessation for ten days. The growth of the uterus is normal for the period. (a) Is such a bleeding compatible with the survival of the fœtus? (b) What can be the cause; a sort of placenta prævia? (c) What will be the course of this pregnancy? (d) How should I tackle the problem of treatment?

REPLY.—In searching for the cause of bleeding in this case, placenta prævia, multiple pregnancy, and hydatidiform mole must be considered. It is assumed that cervical pathology has been excluded by speculum examination. If facilities are available, valuable information might be obtained from a quantitative Zondek-Aschheim test and estimation of the urinary pregnanediol. These tests would not only assist in excluding hydatidiform mole and multiple pregnancy but the latter would be useful in deciding if the administration of progesterone is necessary. Recent work suggests that this substance, when given in cases in which the excretory level is within normal limits, is not only harmful but may accelerate the abortion. It is impossible at this stage to assess the outcome of the case, and the fœtus may well survive and continue to develop normally despite many episodes of hæmorrhage and discharge. The attitude should be that of "wait and see", always bearing in mind the possibility of placenta prævia as a later complication. As a further precaution in the later months, X-ray of the fœtus would be advisable to exclude an abnormality. In the immediate treatment, emphasis must be placed on conservative measures. Absolute rest should be recommended while the bleeding continues, and all unnecessary local trauma in the form of pelvic examination and coitus should be avoided. Mild sedatives might prove of value, and vitamins, particularly synthetic vitamin E in large doses, are worthy of trial.

R. L. HARTLEY, M.D., M.R.C.O.G.

The Headache of Intracranial Neoplasm

QUERY.—What significant features in an account of headache would suggest the possibility of an intracranial neoplasm? I am not referring to physical signs.

REPLY (from a neurologist).—Significant features are (a) intermittent occurrence, (b) severe bursting character; (c) aggravation by coughing, straining at stool, or physical effort, (d) association with vomiting.

PRACTICAL NOTES

Snoring

SNORING, says Ian G. Robin (*Proceedings of the Royal Society of Medicine*, March 1948, 41, 151) "is a symptom of unbalanced breathing, caused by a combination of several physical conditions . . .". Organic causes of snoring are (1) nasal obstruction, and (2) pathological changes in the pharynx. Snoring may also be due to functional dysfunctions of the central reflex governing the tone of the glosso-pharyngeal musculature. The basic cause of snoring is, of course, mouth-breathing. There are three main groups of snorers—the child, the adult and the elderly person. In the majority of children cure can be obtained by removal of adenoids and tonsils; the failures include persistent mouth-breathers and children with infective or allergic rhinosinusitis. When snoring starts in an adult it is usually due to some organic cause. The third group, elderly men and women, is the largest, and the fundamental causal factor seems to be lack of tone. *Treatment* is classified under three headings:—(1) Irrational methods, chief among which is amputation of the uvula. This rarely gives relief, but may modify the degree and pitch of the snore. (2) Rational methods: (a) the removal or prevention of nasal obstruction so as to obviate mouth-breathing. In some cases the application of decongestive nasal drops before retiring produces a peaceful night; in others nasal operation may be necessary; in some benadryl therapy is beneficial. (b) Change of position of the head to prevent the tongue from falling back. In many persons snoring occurs only when they lie on their backs, and this can be prevented by sewing a cotton reel into the back of the pyjamas or nightdress. (c) Alteration of the position of the tongue, soft palate and jaws, by breathing, swallowing and phonetic exercises, or by the wearing of orthodontic splints. (d) Keeping the mouth closed during sleep, by wearing an "Andresen" splint, or by placing a strip of adhesive plaster across the corner of the mouth. (3) Altering the texture of the soft palate and faucial pillars, by injection of a sclerosing solution into the pillars. This method, advocated by Jerome Strauss, has so far failed to produce a high percentage of cures. In conclusion, the author states that many a potential snorer may have been prevented by the removal of tonsils and adenoids.

Tonsillectomy in Childhood

In a critical review of the literature on the subject of tonsillectomy in children, J. Alison Glover (*Archives of Disease in Childhood*, March 1948, 23, 1) draws attention to the fact

that in the last twenty years "far more than one and a half million tonsillectomies have been done on elementary school children in England and Wales". Its frequency in children of the well-to-do is more than three times as high as in children at elementary schools. For instance, at Eton in 1938 some 83 per cent. of new boys had been tonsillectomized before entry. "In general, the wealthier and more exclusive the school the higher is the tonsillectomy rate, and for a boy 'to be born with a silver spoon in his mouth' seems to be one of the conditions which lead to tonsillectomy". Glover summarizes the position as follows:—The most reliable indication for tonsillectomy in children is the occurrence of repeated attacks of acute tonsillitis which cannot be explained by extraneous infection. Bronchitis, asthma and nephritis are contra-indications. The value of tonsillectomy in acute rheumatism is doubtful. To remove the tonsils to cure sinusitis is to put the cart before the horse. Tonsillectomy has no value as a prophylactic against common infectious diseases, with the possible exception of diphtheria. The operation is never urgent. It should not be done in winter or early spring, or during the prevalence of infectious diseases, especially poliomyelitis, measles and influenza.

The Sedimentation Rate in Asthma in Children

In 33 children with asthma who were submitted to irradiation with radon the sedimentation rate was determined before, during and after treatment (S. Livingston: *Bulletin of the Johns Hopkins Hospital*, March 1948, 82, 385). In 15 patients who were relieved completely of their asthma after radon therapy, the average sedimentation rate before treatment was 29-28 mm. per hour; during treatment 16 mm. per hour, and after treatment 6 mm. per hour. In 7 patients who were markedly or moderately relieved of their asthma after radon therapy, the average sedimentation rate before treatment was 18-24 mm. per hour; during treatment 12 mm. per hour, and after treatment 8 mm. per hour. Eleven patients did not respond to radon therapy, and in this group the average before treatment was 5-4 mm. per hour; during treatment 5 mm. per hour, and after treatment 2 mm. per hour. It is concluded that determination of the erythrocyte sedimentation rate may prove useful in deciding which children will benefit by irradiation, and may also serve to differentiate between infective and non-infective asthma. Further, it was found that in all the cases which responded favourably to radon

irradiation there was complete disappearance of lymphoid tissue in the nasopharynx, and in all but one case the sedimentation rate, which was high before treatment, returned to normal after completion of therapy. The period of observation after completion of the radon therapy was from six months to four years.

Hormone Therapy in Peptic Ulcer

THE observation that peptic ulceration occurs four to five times more frequently, and its complications ten to fifteen times more frequently, in men than in women has suggested its treatment with sex hormones. A. Wagner (*Klinische Medizin*, March 15, 1948, 3, 217) since 1940 has treated 157 patients, aged eighteen to seventy, with gastric and duodenal ulcer by means of sex and suprarenal hormones: 124 with sex hormone (two-thirds, menformon-folliculin; one-third, cyren), 11 with androgen, 12 with per corten, and 10 with a combination of prosplen-cyren B forte. The following dosage was employed: after the third or fourth day in hospital 8,300 I.E. menformon-folliculin daily for eight to ten days; seven patients received 25,000 I.E. daily for seven days, or 50,000 I.E. for six days, followed by 10,000 I.E. for eight days. Of the 124 cases, no niche could be seen after four weeks in 75, and they were free from complaints; 8 after two months showed no X-ray improvement, and 4 of these were free of pain in the fifth week only. In 41 patients the niche took more than five weeks to heal. In a quarter of the cases there was recurrence within two years. Menformon acts more promptly than cyren. Optimum dosage is important, for large doses retard healing. Leucocytosis accompanying correct dosage may be interpreted as a suitable response to hormone therapy.

Translucency of the Breasts as an Early Test of Pregnancy

ACCORDING to L. Halberstaedter (*Journal of Obstetrics and Gynecology of the British Empire*, February 1948, 55, 65), the translucency of the normal breast diminishes during pregnancy, and this sign can be useful in some cases as a quick and easy method of differentiating between pregnancy and other processes, but only if it is clearly positive. To carry out the test, Halberstaedter uses a small electric bulb of 6 to 8 volts, fixed at the end of a curved rod and connected with a small transformer (15 to 20 watt). The intensity of the light is regulated by a rheostat and adjusted to the size of the patient's breast. The examination is carried out in a dark room after adaptation of the examiner's eyes. It is stated that in the first 6 weeks of pregnancy the breasts are still clearly translucent. Between 6 and 10 weeks the translucency begins to

diminish, but experience is required to decide the degree of reduction of translucency in this period. After 10 weeks the fading of translucency is easier to determine, and after 12 weeks the breasts are practically always opaque.

The Treatment of Diabetes Insipidus with Pituitary Implantation

THE successful treatment of a case of diabetes insipidus complicated by severe adiposity is recorded by F. E. Schertenleib (*Praxis*, March 25, 1948, 37, 209). The patient was a fifty-three year old woman with severe generalized adiposity and diabetes insipidus, with polydipsia, and polyuria (11 litres per 24 hours). The obesity was so severe that the patient was practically immobilized: it was successfully treated by diet and thyroxine therapy, the weight thereby being reduced from 136 kgm. to 120 kgm. Posterior pituitary extract was given without any satisfactory effect on the diabetes insipidus. An injection of fresh calf pituitary was then injected into the gluteal muscle, with good results. After ten days, however, the condition relapsed and two fresh calf pituitary glands were implanted intragluteally. The result was dramatic; one hour after the implantation the thirst had disappeared; the specific gravity rose to 1027, and the twenty-four hour urine amount fell to 300 c.cm. There had been no relapse at the time of recording the case, seven months after the implantation.

Combined Diphtheria, Tetanus and Whooping-Cough Immunization

ONE HUNDRED AND TWENTY-SIX infants and children, of ages ranging from six months to six years, were immunized with combined diphtheria and tetanus toxoids (aluminium hydroxide adsorbed) containing *H. pertussis* vaccine. The results are recorded by J. J. Miller and M. L. Ryan (*Pediatrics*, January 1948, 1, 8). The children were divided into two groups, one group receiving two injections of 1 c.cm. of combined toxoids each containing 20 billion *H. pertussis* (this group comprised 64 boys and 62 girls), and the other group (54 boys and 49 girls) receiving, in addition to the total of 40 billion *H. pertussis* in the combined toxoids, an additional injection of *H. pertussis* vaccine, bringing the total up to 60, 70, 80 or 100 billion. An interval of 12 weeks was allowed between the two injections, and the extra injection of *H. pertussis* given to group 2 children, was given midway between the two injections. No re-injections were made during a four-year period. Two cases of whooping-cough occurred among the children in group 1; none was known to occur in group 2. Pertussis agglutinative reactions consonant with clinical immunity were

obtained in 70 per cent. of children during the first year after injection; in the subsequent four years serological immunity waned to 40 per cent. High levels of tetanus antitoxin were found during the first year, and levels of 0.1 unit or more were maintained in 98 per cent. of children from two to four years thereafter. Shick tests were uniformly negative, and re-testing at two to four years also produced negative results. Diphtheria antitoxin titrations performed before Shick testing showed a level of 0.1 unit or more in 90 per cent. of subjects. Observation for two-and-a-half years of the children to whom extra dosage of *H. pertussis* vaccine was given between the two injections of triple mixture, showed that high agglutinative titres were thus produced in 84 per cent. of children. The tetanus and diphtheria antitoxin titrations in this group were similar to those in the first group of children, and no positive Shick tests were found.

The Sedimentation Rate in Ulcer and Cancer of the Stomach

AN estimation of the sedimentation rate in 110 cases of cancer of the stomach, 90 cases of gastric ulcer, and 100 cases of duodenal ulcer has been made by B. Rilliet, at the Medical Clinic of the University of Geneva (*Revue Médicale de la Suisse Romande*, March 25, 1948, 68, 158). It was found that in 80 per cent. of cases of carcinoma of the stomach the rapidity of the sedimentation rate was accelerated, but as similar results were obtained in the cases of gastric ulcer it is considered that in cases in which clinical and radiological examination leave the differential diagnosis in doubt the determination of the sedimentation rate has little value. Nevertheless, in cases of carcinoma of the stomach with metastasis the sedimentation rate is usually much more rapid than in those cases which can be considered operable. Van Hees, however, recommends in cases of ulceration of the stomach a therapeutic trial with control of the rapidity of the sedimentation rate; if the case is one of ulceration, the sedimentation rate sinks rapidly, whereas in the presence of cancer the sedimentation rate remains as rapid as at the beginning of treatment. In four cases out of five of duodenal ulcer, the sedimentation rate will be found to be normal.

Exfoliative Dermatitis due to Codeine

A CASE of exfoliative dermatitis occurring in a man of thirty-four years who, before admission with a diagnosis of scarlet fever, had been treated for six weeks for severe myositis with large daily doses of codeine in conjunction with other drugs, is recorded by J. H. Moyer (*New England Journal of Medicine*, April 1, 1948,

238, 469). A mild generalized erythematous rash with superimposed urticaria had developed seven days before admission, but subsided after two days. Four days later, however, the rash recurred accompanied by fever, the temperature being 104° F. The urticaria was followed by weeping and generalized desquamation, and on the twelfth hospital day a secondary skin infection developed on the legs with rise of temperature, leucocytosis and regional lymphadenitis. Penicillin, 40,000 units three-hourly and tyrothricin locally brought the temperature to normal within five days, and the condition gradually improved. After convalescent tests with phenobarbitone, thiamine and salicylate were carried out and proved negative but 30 seconds after an injection of codeine 1:10,000 solution, a generalized urticaria developed, which subsided leaving a marked purpuric spot at the injection area, similar to the condition noted on admission. Similar cases of the occurrence of an erythematous scarlatiniform rash following codeine administration have been recorded in the literature; but the reported case was particularly severe, the toxic condition running a severe course for forty days with the complications of diplopia and secondary infection.

The White Cell Count in Syphilis

IMPRESSED by the contradictory statements in the literature concerning the white cell count in syphilis, R. R. Willcox (*Journal of the Royal Army Medical Corps*, February 1948, 90, 61), has analysed the white cell counts in 405 male Service patients with early syphilis. These consisted of 166 cases of sero-negative primary syphilis, 164 cases of sero-positive primary syphilis, and 75 cases of secondary syphilis. The average count of all cases was: total white cells 8,950; neutrophils 5,560 (62 per cent.); lymphocytes 2,830 (31.5 per cent.); large mononuclears 410 (4.5 per cent.); eosinophils 125 (1.5 per cent.); basophils 25 (0.5 per cent.). No gross distinctions were noted between sero-negative primary, sero-positive and secondary syphilis. For instance, the total white cell count for these three groups was 8,850, 9,050 and 9,000 per c.mm., respectively, whilst the percentage of cases in each group with a total count exceeding 12,000 per c.mm. was 12, 18.3 and 13.3, respectively. Similarly with the lymphocytes there was only a slight rise which was not statistically significant:—

		Per cent.
Sero-negative primary syphilis	2,760	31
Sero-positive primary syphilis ..	2,870	31.5
Secondary syphilis	2,900	32

A lymphocyte count of 40 per cent. or over occurred in only 13.25 per cent. of sero-negative primaries, 17.1 per cent. of sero-positive primaries, and 18.7 per cent. of secondary cases.

REVIEWS OF BOOKS

Modern Trends in Dermatology. EDITED BY R. M. B. MacKENNA, M.D., F.R.C.P. London: Butterworth & Co. (Publishers) Ltd., 1948. Pp. xiv and 432. Figures 32. Price 42s.

UNDER Dr. MacKenna's editorial guidance and planning an important work has been evolved, which covers not only the clinical aspects, but ropounds and elucidates those fundamentals of the subject without an understanding of which there can be no progress. A galaxy of contributors, mostly, and refreshingly, not dermatologists, discuss their subjects brilliantly. Clinicians and empiricists abound and they have their place; but advances in dermatology will come only from observations logically based on a sound knowledge of the fundamentals. So much of basic importance is a muddled mystery to clinicians that a catalogue of the chapter headings and their authors alone should suffice to persuade any dermatologist seeking the light to buy this book. When most of the chapters are so good it may be invidious to pick out for particular mention some that seem outstanding: Professor Marrack, on dermatology and nutrition; Professors Peters and Thompson on the biochemistry of the skin; Dr. Barber on the influence of the sex hormones on the skin, with discussion of the "seborrhœic" eruptions, and Dr. Weddell on the anatomy. Personal bias, of course, rather than individual merit, may account for the special appeal of these chapters. Criticism can be levelled at certain features, but this would be to cavil. The book, to which justice cannot be done in a short review, is recommended with genuine enthusiasm to all dermatologists, established and embryo.

Clinical Ophthalmology for General Practitioners and Students. BY H. M. TRAQUAIR, M.D., F.R.C.S. Ed. London: Henry Kimpton, 1948. Pp. xii and 264. 72 illustrations, 8 in colour. Price 25s.

THIS book is an attempt to present ophthalmology in a restricted and elementary manner, and throughout emphasis is more on subjective complaints than on objective findings. There are excellent chapters on history taking, methods of examination, diagnosis, general therapeutics, the relationship of headaches to refractive errors, and on squint. The chapters on external diseases of the eye are simply and attractively written and well illustrated; methods of treatment are discussed only very briefly, and those cases likely to benefit by more expert treatment are clearly indicated. There follows a chapter

on impairment of sight without obvious external signs, in which differential diagnosis is discussed without reference to ophthalmoscopic examination. One feels that this method of presentation is perhaps rather anachronistic and that some familiarity with the technique of ophthalmoscopy could safely be encouraged. The eye changes in nervous and general medical diseases, functional manifestations and conditions peculiar to the extremes of life are briefly described and the book ends with some very pertinent remarks on misconceptions and prejudices. Within its self-imposed limitations the book will be most useful, and it could scarcely be written in a more simple and attractive manner.

Clinical Endocrinology and Constitutional Medicine. BY A. P. CAWADIAS, O.B.E., M.D., F.R.C.P. London: Frederick Muller Ltd., 1948. Pp. iv and 362. Illustrated. Price 42s.

THIS book attempts the difficult task of setting endocrinology in its proper relationship to constitutional medicine, namely as an important and integral part of the study of the individual as a whole. The theme is elaborated with the help of evidence from the study of genes and organizers, of morphology and physiology, of psychiatry and philosophy. The clinical features of the various endocrine syndromes are rightly stressed and their explanation is sought in terms of physiology and pathology, rather than by taking as a starting-point physiological principles and attempting to fit clinical observations to them. This precedence of clinical science would be a more telling feature of the book if the descriptions of the disorders were not rendered colourless by a plethora of technical terms and composite words. Many physicians will deplore the continuance of the dangerous doctrine that sugar as well as insulin should be given to a diabetic in coma. They will also be surprised to read that whole pituitary gland and adrenal cortex by mouth are recommended, and few will agree that endocrinotherapy is as highly specialized as neurosurgery, and thus is not for general practice.

Diseases of the Breast. BY SIR CRISP ENGLISH, K.C.M.G., F.R.C.S. London: J. & A. Churchill Ltd., 1948. Pp. vii and 126. Price 8s. 6d.

THIS is a book of only 126 pages and in it the author sets out quite simply the anatomy of the breast, and an account of the various

diseases which affect the organ. The questions of diagnosis, treatment and prognosis are dealt with. The vital importance of the early diagnosis and drastic treatment of cancer of the breast by radical operation and deep X-ray therapy or radium are rightly stressed. The book is easy to read—the references are set out very briefly and there is no abstruse pathology. It can be recommended to anyone who wishes to read about diseases of the breast from the point of view of a surgeon who has dealt with them through many years of active practice.

Modern Plastic Surgical Prosthetics. By ADOLPH M. BROWN, M.D. London: W. Heinemann (Medical Books) Ltd., 1947. Pp. xiv and 293. Figures 180. Price 35s.

THIS is a valuable and highly specialized monograph on a complicated and little known subject. The book sets out, in part one, the equipment needed in a modern plastic laboratory, and in part two describes the author's techniques in examining patients, and obtaining casts from which to make the finished prosthesis. In part three, details are given of various cosmetic restorations, and in part four, the different materials used and their properties are discussed. The work is profusely illustrated, and there is a good bibliography and index. The photographs are of high quality, and the prosthetic appliances illustrated are excellent. The book can be described as a valuable and helpful reference work on this difficult but valuable aspect of surgery.

Dermatoses Among Gas and Tar Workers.

By W. D. JENKINS, M.R.C.S., L.R.C.P. Bristol: John Wright & Sons Ltd., 1948. Pp. 54. Figures 19. Price 25s.

THIS monograph records the result of observation over a period of ten years of over 6,600 workers in a large gas concern. The industrial processes are described. The employees are divided into groups of workers in the gasworks proper, in the associated tar works, chemical works, coalite works, and those concerned in distribution of the gas. A great variety of occupations is included. The incidence of simple industrial dermatitis was low, and the main part of the monograph is devoted to pitch warts and epithelioma. The frequency of these lesions is in proportion to the degree and duration of exposure, although personal idiosyncrasy also plays a part. Incidence is highest in the tar works, where 365 papillomas and 8 epitheliomas appeared in 63 workers out of a total of 234 at risk. Of 3,034 concerned with distribution, where tar exposure is minimal,

only 5 papillomas and one epithelioma occurred. Lesions were situated almost exclusively on the face, scrotum, backs of the hands, and on the forearms. In prevention, barrier creams were not found of much value, and washing with soap and water is chiefly advocated. The education of workers and encouragement of early reporting of suspicious lesions are important. The monograph contains detailed information regarding *case histories and statistics of incidence*, but general conclusions do not differ from accepted opinion.

Nutrition and Diet Therapy. By AGNES PAVEY, S.R.N., D.N. London: Faber and Faber Ltd., 1948. Pp. 304. Price 12s. 6d.

THE author has added a useful handbook to the few on this subject for nurses. Part one covers the field of nutritional requirements from infancy to old age, with due regard for the present ration system. There are also some good observations on the serving of meals to patients, which will be valuable to members of the nursing profession. The reader is left to guess what is meant by the author's statement that overeating of protein may cause bodily harm. Part two contains good practical information on the dietary treatment of disease and sickroom cookery, although the author quotes the popular belief that the loss of meat juices is less when meat is plunged into boiling water for five minutes than when it is placed in cold water and brought to boiling point. The truth is that the loss by outward diffusion is the same whichever method is employed. The book is well planned and contains useful food tables for the serving of average helpings of the common articles of food.

The Selected Writings of Benjamin Rush.

EDITED BY DAGOBERT D. RUNES. New York: Philosophical Library, 1947. Pp. xii and 433. Price \$5.00.

TO many, Benjamin Rush is merely known as one of the leading physicians in America in the 18th century. There are few who realize that this professor of the institutes and practice of medicine in the University of Philadelphia was also a member of the Revolutionary Congress which in 1776 passed the Declaration of Independence, and that he spent the last fourteen years of his life as Treasurer of the National Mint. A close friend of Thomas Paine, he was in the forefront of the events which led up to the signing of the famous Declaration, and indeed he is said to have suggested the title for Paine's historic pamphlet, "Common Sense". In this selection from his writings, published to

commemorate the bicentenary of his birth, the editor has included examples of both his political and his medical works, under the headings of "On Good Government", "On Education", "On Natural and Medical Sciences", and "On Miscellaneous Things". The fiery zeal of the born radical shines through all the writings, but in those dealing with medical matters there is a breadth and boldness of outlook which renders them almost topical in their outlook at the present day. This is a book which will appeal to all those who are interested in the advance of the practice of medicine.

NEW EDITIONS

MUCH new material has been added to *Diseases of the Eye*, by Sir John Parsons, C.B.E., D.Sc., F.R.C.S., F.R.S., and Sir Stewart Duke-Elder, K.C.V.O., D.Sc., Ph.D., M.D., F.R.C.S., in its eleventh edition (J. & A. Churchill Ltd., 30s.), outstanding among which are the extended use of the sulphonamides and penicillin. As the authors state in the preface, the advent of penicillin has to a large extent revolutionized the treatment of many ophthalmic conditions, and the methods of its use will be found in the chapters concerned as well as in a separate section of the appendix. The new edition is well produced.

WELL produced and well illustrated the second edition of *Diseases of the Chest*, by Robert Coope, M.D., B.Sc., F.R.C.P. (E. & S. Livingstone Ltd., 25s.) contains a most useful chapter on industrial diseases of the lungs. The importance of early diagnosis in pulmonary tuberculosis and helpful suggestions on the rehabilitation of tuberculous patients are other features of the new edition. There is no mention of the use of streptomycin in pulmonary tuberculosis.

Midwifery, by Ten Teachers, edited by Clifford White, M.D., F.R.C.P., F.R.C.S., F.R.C.O.G., Frank Cook, F.R.C.S., F.R.C.O.G., and William Gilliat, C.V.O., M.D., F.R.C.P., F.R.C.S., F.R.C.O.G., in its eighth edition (Edward Arnold & Co., 20s.) is the first edition of this well-known work in which the name of the late Sir Comyns Berkeley, the original author and editor, does not figure among the contributors. The new edition, in the compilation of which all ten contributors have brought their chapters up to date, is a worthy successor to its predecessors.

Introduction to Psychiatry, by W. Earle Biddle, M.D., and Mildred van Sickle, B.S., R.N., in its second edition (W. B. Saunders Co. Ltd., 14s.) has been revised in many sections and more emphasis has been laid on occupational and recreational therapy. Although written largely from the nursing viewpoint, the work should be

of considerable interest to students and practitioners, especially as it gives insight into the methods obtaining in the United States.

OWING to the many advances in surgery since the appearance of the previous edition in 1929 of *Recent Advances in Surgery*, by Harold C. Edwards, C.B.E., M.D., F.R.C.S., much new material has been added to the third edition (J. & A. Churchill Ltd., 24s.). In the chapter on the surgery of the heart a section is devoted to the Blalock-Taussig operation for congenital pulmonary stenosis; in Part IV on the nervous system a separate chapter is given to prefrontal leucotomy; in the chapter on antibacterial therapy the antibiotics are dealt with in detail; and the whole of Part VII is devoted to radiotherapy in malignant disease. The new edition is well illustrated, and each chapter concludes with a useful bibliography.

The British Encyclopædia of Medical Practice: Medical Progress and Cumulative Supplement, 1948. Edited by Lord Horder, C.C.V.O., M.D., F.R.C.P. (Butterworth & Co. (Publishers) Ltd., 1948. 37s. 6d.). Among the many advances included in the 1948 issue of *Medical Progress* are the treatment of essential hypertension by sympathectomy, the surgical treatment of congenital pulmonary stenosis, and much information on penicillin and streptomycin, concerning resistance to the former drug and the toxic effects of the latter. Further information on these subjects is given in the *Cumulative Supplement*.

Practical Food Inspection. Vol. II: Fish, Poultry and Other Foods, by C. R. A. Martin, F.R.San.I., in its third edition (H. K. Lewis & Co. Ltd., 18s.) contains particulars of new legislation in the chapter on legal procedure, and in the chapter on milk and milk products methods of sterilization and pasteurization and the technique of tests for milk examination are included. Inspection of fish, poultry and game and their selection for human consumption are discussed, and there are chapters dealing with canned foods, fruit, vegetables and cereals. There is also an interesting chapter on food poisoning.

Diseases Affecting the Vulva, by Elizabeth Hunt, M.D., Ch.B., in its third edition (Henry Kimpton, 25s.) contains new sections on ulcers due to anaerobic streptococci, and on telangiectases. Other additions include the use of penicillin and the sulphonamides, podophyllin resin in condylomata acuminata, benzocaine as an external agent, and the vitamins.

NOTES AND PREPARATIONS

NEW PREPARATION

"PARAMISAL" brand para-aminosalicylic acid is now available for clinical trial in the form of a sterile 20 per cent. solution for intrapleural injection in tuberculous empyema. The manufacturers are Herts Pharmaceuticals Ltd., Bessemer Road, Welwyn Garden City, from whom further particulars can be obtained.

FOLIC ACID. The price of "Folvite" folic acid (Lederle) preparations, and "Folvron" folic acid and iron tablets, has been reduced by approximately 25 per cent., and freed from purchase tax. The distributors are Cyanamid Products Ltd., Brettenham House, London, W.C.2.

AIR TRANSPORT AND MEDICAL RESEARCH

B.O.A.C.'s fast Lancastrian freight and mail service now makes it possible to transport heat-labile products to countries 12,000 miles apart. This is a great benefit to medical research. Recently a consignment of dried cultures of bacteria (*Staph. pyogenes*) sealed in glass ampoules, and bacteriophage in fluid packed in dry ice, from the Central Public Health Laboratories in London, was flown from London Airport to Sydney, for delivery to the Institute of Medical and Veterinary Science, Adelaide, South Australia. The dry ice was renewed by B.O.A.C. staff en route at Lydda, Calcutta, Singapore and Sydney, and the carton arrived safely at its destination "with dry ice to spare", the journey having been completed in approximately four days.

ROYAL SOCIETY OF ARTS: SWINEY PRIZE

THE Council of the Royal Society of Arts give notice that the next award of the Swiney Prize will be made in January, 1949. The award is made by a joint Committee of the Royal Society of Arts and the Royal College of Physicians, which appoints special adjudicators. The prize will be presented to the author of the best published work on Medical Jurisprudence. Any person desiring to submit a work in competition, or to recommend any work for the consideration of the Judges, should send it to the Secretary of the Society, John Adam Street, Adelphi, London, W.C.2, not later than November 30, 1948.

PUBLICATIONS

British Journal of Plastic Surgery.—The first issue of this new quarterly journal is as outstanding for its excellence of production as for the high standard of the articles. Among the contributors are Sir Harold Gillies, Sir Archi-

bald McIndoe, and Professor Paterson Ross. The publishers are E. & S. Livingstone Ltd 16 and 17 Teviot Place, Edinburgh. Annual subscription two guineas.

Medical Research in War is the Report of the Medical Research Council for the years 1939-45. This is perhaps one of the most interesting and far-reaching of the Council's publications. In the chapter on therapeutics there is an extensive section devoted to penicillin; in the chapter on wounds and injuries are sections dealing with nerve injuries and traumatic shock; blood transfusion, health research in industry, and the use of BAL in poisoning by metals are other subjects of topical interest. The Report is published by H.M. Stationery Office, price 7s. 6d.

Males and Females, by Roger Pilkington, is written primarily for adolescents and young adults. In a refreshingly original manner the author succeeds in presenting a simple, yet reliable description of human reproduction from the angle of heredity. The book will appeal to all who are concerned with the vitally important problem of sex education. It is published by Delisle Ltd., price 6s.

MEDICAL FILMS

A FILM strip dealing with "The Diagnosis of Threadworm Infestation" by Dr. B. Stanford, under the direction of R. C. Mac Keith, D.M., M.R.C.P., D.C.H., and J. M. Watson D.Sc., A.R.C.S., drawings from which appeared in an article by these authors in *The Practitioner*, April 1948, 160, 264, is available from the British Industrial Films Ltd., 177 The Vale, Acton, London, W.3. Other medical film strips are in process of production. Film strips in black and white are obtainable at 10s. per copy, and those in colour at 20s. per copy.

"PROGRESS AFOOT" is a film dealing with flat feet, with special reference to the constructions of the "inertez" shoe. This shoe for children, which is supplied on medical prescription only, incorporates the necessary alterations for the treatment of flat feet by means of in-built wedging. Details as to time and place of the showing of the film can be obtained from the Managing Director, James Southall & Co. Ltd., 34 St. George's Street, London, W.1.

INDEX TO VOLUME 160 (JANUARY-JUNE 1948)

The index to Volume 160 will be dispatched to subscribers with the July number. Binding cases in green cloth will also be ready by July 1, and are obtainable at 4s. post free.

The contents of the July issue, which will include a symposium on "Social Medicine", will be found on page lxxiv at the end of the advertisement section.

THE PRACTITIONER

Edited by

SIR HENEAGE OGILVIE

8 K.B.E., D.M., M.Ch., F.R.C.S.

and

WILLIAM A. R. THOMSON
M.D.



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